Viral Replicat°

1- Adsorpt° (Attachment), to specific (Rs)
2- Entry (Penetrat°)
3- unCoating: removal of Viral Coat by Cellular enzymes → Nucleic acid Release. (Release)

4- Eclipse   5- Assembly   6- Release.

Inclusion bodies:

. Spherical; (7 μm) Represent site of Viral Replicat°

. It may be
1- IntraNuclear: HHV & HPV
2- Intra Cytoplasmic: pox Virus.

Cut. Viruses

DNA
- intranuclear: HHVs, HPV
- intracytoplasmic → PoX

RNA
- Picorna (Coxsackie) ← HFMD
- RetroViruses: HTLV & HIV.

Coxsackie
Coxsackie
Picorna

Human Herpes Virus group.

- Herpes: Greek word means "To Creep or Crawl" in Reference to the spreading Nature of the dis.
- Herpetiform: lesion that is similar to HSV (multiple grouped vesicles on erythematous base or similar to Herpetic ulcer). [painful, superficial Erosion]

- Human Herpes Virus group ch BY:

① : double stranded DNA
② . Replicate intranuclear.
③ . Produce: 1ry infect → Latency → Reactivat. & Recurr. inf.
- 1ry infect: at site of inoculat
- Latency: in Nervous or Lymphoid Tissues.
- Reactivat. & Recurr. inf.: in Later life either spont. or by Rpt. agents

Classification of Human herpes viruses "HHVs"

HHV 1	Skin & oral mucosa → H. labialis.
HHV2	Genital areas → genital herpes.
HHV, 3	Varicella zoster.
HHV, 4	Epstein-Barr virus. → IMN & Gianotti Crosh
HHV, 5	Cytomegalovirus CMV
HHV, 6	Exanthem subitum (roseola infantum). / DRESS
HHV, 7	Associated with roseola.
HHV, 8.	Associated with KS. / Lymphoma, Multicentric Castleman's dis. (Lymphoprolif. dis ch BY Fever, LN, HSM)

2 Ass

	HHV	Site of latency	Manifestations	
α-HV	HHV1 (HSV1)	Nervous syst. "Neurons"	H. labialis	1° & recurrent
	HHV2 (HSV2)		Genital herpes	
	HHV3 (VZV)		Chicken pox	1°
			H. zoster	2°
β-HV	HHV5 (CMV)	Immune syst. "Lymphoid tissue"	Asympt. mono-like	
	HHV6		Roseola infantum ✓	
	HHV7		Associated with Roseola ✓	
γ-HV	HHV4 (EBV)		Infectious mononucleosis. (IMN)	
	HHV8		KS associated herpes virus	

pit Rosea dress Synd

Herpes Simplex Viruses

(HSV1 & HSV2)

- Non genital H-SV
- usually affect Non genital skin & MM.
  ↓
  Herpes labialis (Above Waist inf.)

- Genital HSV.
- usually affect Genital skin & MM.
  ↓
  Herpes Genitalis (Below Waist inf.).

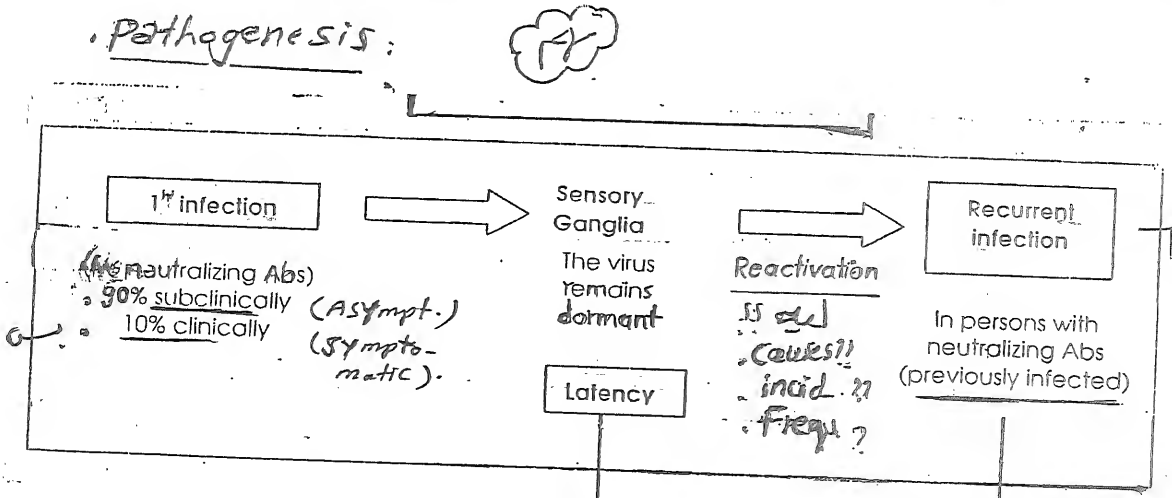
NB • Nowadays HSV1 may affect the Genitalia (10-40%) & HSV2 may affect non Genital skin & oral MM (d.t Common practice of oral sex).

• Both produce Multiple grouped vesicles on Erythematous base at ...

• **Mode of Transmission:**

1. droplet inf. (in HSV1 labialis)
2. Contact with < active lesions (vesicular lesions before crusting) / infected secretions.
3. Sexually Transmitted (HSV1 & HSV2) < oral sex / intercourse
4. [placental] = Vertical Transmission (From mother → fetus)

• **Pathogenesis:**



Site of latency

- HSV1 → Trigeminal Ganglion
- HSV2 → Lumbo-sacral Ganglion (Hip, buttocks, genitalia, L.L)

- So may reinfect:
  - face
  - Oropharyngeal MM
  - ocular MM

Comment on:-

- Types (CIP)

Types of Inf. Caused By HSV

- **Initial or first Episode Inf.**
  - **1ry** (True 1ry inf.) → Never infected by HSV1 Nor HSV2
  - **Initial Non 1ry inf.** → individual previously infected by one type & develops inf. by the other type.
- **Recurrent inf.**
  - clinically .3 Types
    1- Symptomatic (<50%)
    2- Symptomatic unrecognized
    3- Asymptomatic
    (>50%)

Clinically: 10% Sympt. & 90% Asymptomatic

- **Reactivation:**
  - Causes of reactivat
  - incid.
  - No of Recurrences/y
  - C/P

(4)

(1)

- **Causes of Reactivat:** either
  1. Spontaneous
  or 2. predisp. factors: (i) [Stress, Sex, Menses] (ii) [Fatigue, Fever] (iii) [UVB (HSV1), Immuno-Suppression]

Reactivat	HSV1	HSV2
(2) Incid.	≃ 50%	≃ 90%
(3) No of Episodes	≃ 1 / Year	≃ 6 / Year

So HSV2 recurs more Common & more frequent > HSV1

Types of Recurrent inf.

1. **Symptomatic**: classical lesions & symptoms of HSV.
2. **Asymptomatic** (No S. nor S) (subclinical): the virus descends from the dorsal routes along the nerve & replicate at skin surface or MM ēout producing lesions or symptoms.
3. **Symptomatic unrecognized**: المريض بيجيله عنده أعراض بسيطة احمرار أو شكوى على الجلد وميش بيعرف إنها HSV إلا لما يروح لدكتور (non classical S & S of HSV inf.)

↓

So that periods of transmission or shedding of the virus may occurs during:

1. **Symptomatic shedding**: shedding during active symptomatic lesions. ← less common period of transmission.
2. **Asymptomatic shedding** (the virus descend along the nerve → replicate ēout producing lesions): shedding during abscence of clinical lesions.
3. **Unrecognized shedding**: المريض مايعرفشي إنه عنده HSV علشان مش شكل العدوى الكلاسيكي

(2 & 3) → the Main & the Most important periods of Transmission.

Diseases caused by HSV:

1. 2 main diseases:
   - Orolabial H.S (H. labialis orofacialis)
   - Genital H.S (H. genitalis or progenitalis).
2. Other Herpetic inf.:
   - ocular H.S
   - (A) Neonatal H.S (A)
   - Herpetic Whitlow
   - Herpetic sycosis.
   - H. Gliadialerum
   - (B) Eczema Herpeticum
   - H. Encephalitis
   - (C) Herpes in special situations → HIV / Immunocompromised.

الامتحان Q

NB: A, B, C → امتحان

Orolabial H-S (Commonest HSV1 Inf.)

برداية ⊙ Viral Transmission
- HSV1 ++
- HSV2 ±

IP: 3-7 ds.

↓

Primary infection → (Herpetic Gingivo-stomatitis) (MM)

↙ 10% Symptomatic ↘ 90% Asymptomatic

(a) prodromal (marked) <
- Systemic: FAHM, L.N (tender)
- Local: discomfort, burning, Tingling, Numbness & Tenderness

(b) Eruption (lesion): ⊙ presentation acc. to age:
- Vesicles
- Site
- Healing

- Gingivostomatitis: in children (< 10 ys)
- Pharyngitis: in young adults (IMN like)

→ 3 sites: oral mucosa, pharynx, gingivae.

⊙ more numerous, Less grouped Vesicles on erythematous base → rupture → crusted → (2-3 ws) → Resolut

↓

Latency (in Trigeminal Ganglion)

↓

Predisposing factors For Recurrence
Specially UVB (Sun)

Reactivation ↗

↓

Recurrent episode. → (Cold sore, Fever blister)

NB
Skin Vesicle
dome shapped
umbilicated.

(a) prodromal ē as in 1ry inf. but less marked

(b) Eruption (lesion): - fewer No of vesicles + Marked grouping

- Healing ē in 1-2 Ws.

NB Rare Mucosal affect Except Hard palate (Hard Mucosa over Bone) ⊕ Immunosupp. (soft mucosa)

- Site of lesions:
  - Commonest: lip (Vermilion border)
  - Less Common:
    - perioral
    - perinasal
    - cheek
    - ear lobule

(No MM affect)

(d) Recurrence: ≃ 1 / year.

- Note the difference bet. 1ry inf. & Recurrent inf.

سؤال

بين
- Prodroma
- Lesions → No. of vesicles, grouping, site, Healing

- Note that → 1ry orolabial H.S: Called Herpetic Gingivo-stomatitis
  → Recurrent " " ": called → Cold sore = Fever blister

- What is the Commonest predisposing Agents?? Sun (UVB)

1ry infection	Recurrent infection.
- IP: 3 - 7 days	. Reactivation either spont. or under effect of certain Agents.
- usually: children (1-5 ys) or young adults.	. Adults.
- usually: Asymptomatic (90%) & if symptomatic it will be more severe.	. (if) symptomatic → Less severe.
- Prodroma: Marked	. Less marked
- Eruption: (Lesion)	
Ⓐ - more numerous Vesicles & lesser grouping.	- Fewer Vesicles & more grouping
Ⓑ. MM: usually affected	- usually (not) affect the MM. lesion affect the same Region but not the exact area
Ⓒ. Healing: 2-3 Ws	- Healing 1-2 Ws.

Genital Herpes

(Herpes progenitalis)

- Def. infection of Genitalia by HSV.
- AET & Transmission:
  - HSV_2 (70%) → sexual intercourse.
  - HSV_1 (30%) → oral sex.
- Types of infection:
  1- True primary inf.
  2- Initial Non primary inf.
  3- Recurrent inf.
- Periods of Transmission: ± during:
  1- symptomatic inf.

Most cases →
  2- Asympt. shedding
  3- sympt. unrecognized.

CIP

(A) primary inf. (< 90% Asympt. / 10% Sympt)

1- Ip: 2 ds - 2 Ws (usually 3-7 ds)
2- Prodroma < local / systemic
3- lesion (№ & grouping of vesicles).

Site

- Rectum
  - ♂ → Homosex.
  - ♀ → ??
- ♂ → Painful Erosive balanitis
  - Commonest at glans, shaft & rectum (in Homosex.)
  - Vesicular ulcerated lesions.
- ♀ (Bilat).
  - Vulvitis
  - Vaginitis
  - ✓ Cervicitis (Most Common 80-90%)
  - Buttocks/perineal

Healing: 2-3 Ws.

B- Recurrent inf.: (Reactivat.):

1- Reactivat.: cause, incid, No., Types

2- Pradroma ← local (+) / syst. (-) (Mild)

3- lesions (No & grouping of vesicles)

Site: → same Region but not the exact area (generally below Waist).

Healing: 1-2 Ws.

(H. labialis اقل)

NB 1. Recurrent inf. usually (>50٪) ASympt. or Sympt. Unrecognized.

→ 2. Initial Non 1ry inf. is more mild > True primary inf. (شديد)

Complications of H. Genitalis:

- More Common in:
  1- Women 2. 1ry inf.
- include:
  1. 2ry bact. inf. (Most Common) ± → Scarring
  2. Extragenital lesions (20٪) (Cut. or Syst.)
  3. Urine Retention (15٪): d.t.
     - Lumbosacral radiculopathy
     - Reflex pain inhibition d.t intraurethral lesions.
  4. Aseptic Meningitis. (Fever, Headache, + Vomiting & photoph. obia). FAHM (P)
  5. Neonatal H.S.
  6. Cancer Cervix. ← So Recurrent Hs of Cervix → do cytological Smear/Y.
  7. depression / psychosexual problems.

Neonatal H.S

- Mode of Transmission:

1- Antepartum (Transplacental): (10%)

2- Intrapartum: during delivery: (90%) (via Birth Cand.)

3- Postpartum: non maternal source (kissing by infected adult) (10-15%)

(So there are 2 sources: Maternal & non-Maternal).

- Risk of inf

A- Episode: 1st Episode attack of mother is more dangerous > recurrent Episodes in Causing Neonatal inf. Why?? (in recurrent Episodes the fetus is protected by Maternal Igs)

- incid acc. to the Episode:

(1) True 1ry Episode → 50%

(non 1ry 1st episode) → (2) initial non 1ry → 30%

(3) Recurrent episodes & asympt. shedding → 0-4%

B- HSV1 > HSV2 (despite its less common).

C- presence of "active lesions" at time of delivery.

D- PROM

E- using fetal scalp Electrode.

NB: - The most serious is Women (e) 1ry inf. & having active lesion caused by HSV1 at Time of delivery. However most cases are d.t Asympt. shedding.

CIP

Ante partum (Transplacental) (10%)

- Abortion.
- IUFD.
- Prematurity.
- Cong. Anomalies:
  - MicroCephaly
  - MiCrophthalmia
  - limb hypoplasia
  - EnCephalitis
- Skin affect⁻: Extensive Cong. Vesicles & Erosions → Healing & reticulate scarring & usually fetal

Intra partum (Commonest) (90%)

- Types of affect⁻
  1. SEM: localized inf of skin, Eye & mouth.
  2. Localized CNS affect⁻.
  3. Dissominated inf. (Multiple organs) ← CNS, Lung, Renal.
  4. Non Specific Symptoms as: irritability, poor feeding & lethargy.

Complications

- Seizures
- psychomotor retardat⁻.
- Spasticity
- Blindness
- learning disabilities.
- Death.

NB:
- Transplacental Transmission: has poor prognosis & High Morbidity & Mortality
- Intrapartum Transmission: has better prognosis & > 90% develops normally.

DNNZ

ECZema Herpeticum

(Kaposi VariCelliform Eruption)

• HSV inf (1 or 2) + any of the following condition : → spread of HSV throughout the diseased areas (ECZematous Areas)

usually first Episode

- AD
- SD
- scabies
- Ichyosis
- Darier
- Hailey-Hailey (H.H)
- pemphigus.
- pemphigoid.

C/P (DNNZ) :

1. IP : 5-12 ds
2. FAHM
3. Clusters of itchy &/or painful blisters starts usually at head & Neck on active or healed site of previous skin dis (e.g AD) —7-10 ds→ New patches appears at other diseased areas which may become Generalized —2-6 ws→ ± Healing with small white scars.
   - the lesion ch-by: monomorphic, umbilicated vesicles filled with clear, cloudy or Hgic fluid → Hgic crust formation → (Painful punched out bleeding Erosions).
4. 2ry bact. inf. may occur.
5. in Severe Cases → systemic organ affection e.g Eyes, CNS, Lung, Liver → fatal

- Fever
- Severe pain
- vesicles ← Monom. umbil. fluid
- Punched out Erosion
- 2ry bact inf. & disseminat.

→ Clue for Diagnosis

NB: other viruses may cause ECZema Herpeticum:

- Vaccinia virus → ECZema vaccinatum
- Hand-foot & mouth dis → Coxsackie v. A16 → Coxsackium

NB When caused by HSV Af it's called Ecz. Herpeticum but when the causative virus is unknown this called Kaposi Varicelliform Eruption

Treatment: (1) ACV or VCV: oral or IV
(2) Antibiotics
(3) Consult ophthalmologist if Eye affected

NB What is Zostriform HSV??
What is Varicelliform HZ??

chicken pox

أذية
Fluroscence ← **Ocular H.S** (Herpetic Keratoconjunctivitis)

- Keratitis, Conjunctivitis, Corneal ulcer & ± Eyelid affect
- preauricular L.N
- 2nd commonest cause of corneal blindness in USA

Specifically Trifluridin (Viroptic) antiviral

⊙ is it HSV1 or HSV2:

- (التبكيرية) if Neonatal → usually (HSV2)
- if older than Neonate → " (HSV1)

- Pathognomonic: Branching, dendritic lesions of corneal epith.

ع الاصابع **Herpetic whitlow** ??

digital H.S infection occur in:

- children: ē oral H.S] HSV1
- dentists & medical personnels] HSV1
- digital/genital contact → HSV2

سم للمصارعين أثناء الالعاب الرياضية → **Herpes Gladiatorum** (مصارعين)

- H.S infection occurs among wrestlers (لاعبي الرياضة) or during practice of sports d.t close contact.

(H. Folliculis) → **Herpetic Sycosis**: H.S inf. of beard & moustach of Adult → Viral Folliculitis

Herpes infection in special situations (لها مكان)

[A] In immunocompromised: مشاكل ع

1. chr. ulcerative H.S: persistent Erosions & ulcerat in Face & Perianal area. (تقرحم لشكاية)
2. Acute Generalized: (Varicella like): wide spread vesicular Eruption (as Varicella) → death
   - lesion ± : Verrucous, Exophytic, Pustular, ulcerative
3. disseminated Visceral
4. More Frequent shedding
5. ACV Resistant H.S (So) use < Foscarnet, Cidofovir > ← سؤال مشهور

[B] HSV + HIV: → more severe outbreaks; → More Frequent Viral shedding

- use Anti HIV + ACV (if (No) Resistance).

Q. How to differentiate bet. 1ry & Recurrent attacks (See no. 1 above)

Q. Whole durat° of dis outbreaks??
- Primary attack : 3Ws
- Recurrent " : 1w.

Q: does Frequency & Recurrence will ↓ over the time (without tt ??) ??
- over longer periods (3-5 Ys) Frequency of outbreaks will ↓↓.

Q. Why genital Herpes is a problematic disease??
- because it is not curable so → associated ← social stigmata:
  - Emotional stress
  - Anger
  - depression
  - Guilt
- → *(So) psychological aspect should be evaluated well.

Diagnosis of HS

1. Tzanck smear:
- Rapid preliminary procedure that can be used in office
- Nonspecific (Can't diff. bet. HSV1 & HSV2 or even VZV)
- Results: 60-90% accurate, 3-13% False +ve.
- Method: Recently developed vesicle (48hrs) → deroofed → Absorbant Gauze for Fluid → swabbing the base then examined by Mic or stained then examined → Multinucleated giant cells. (Toludine)

(till serum obtained (# Bleeding))

2. DFA: Rapid, sensitive, diff. bet (HSV1) & (HSV2) [الأفضل والأكثر استخدام في الوقت الحالي]

3. Culture: differentiate bet. different types & Can be available within 2-5 days. (on Hela Cells)

4. PCR: good as Culture. used to detect DNA of the virus in CSF

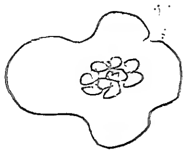
5. serology: 1. detect asympt. carriers. 2. determine inf. Rate in Various Populat°. 3. detect couples at Risk for Neonatal H.S
- In general: IZA (ELISA)
- Western Blot: Very good for detect & Glycoproteins: gG1 → HSV1 & gG2 → HSV2

WB is FDA for detect & prevalence

6. Histopathology : (٢٧)

أدله ما جه يتقطر → ① Ballooning degen of KCs with intra-nuclear Inclusion Bodies (degenerat & Marginat of chromatin)
→ Blistering (at level of st. Spinosum)

② Multinucleated giant Epid. Cells : (Syncytial cells)



. Formed by fusion of infected KCs
. Nuclei are fit or molded together as pieces of puzzle. (ليجو)

(NB) : D depends on lesional Morphology :—

- Acute Vesicular lesion —(do)→ Tzanck.
- Crusted, eroded or ulcerative lesion → others

سؤال Q - Complications of (H-SV1) & 2 سؤال ٢٧ كتطبيرا

① 2ry bact. inf. ↔ scar بسبب
عينيه ② Corneal ulcer, opacity
جسم ③ dissemination → Hepatitis, encephalitis & Pneumonia.
④ HAEM (Herpes ass. Erythema Multiform):
H.S is the Commonest Cause of Recurrent EM
Usually after : (9) days.

أهم (٤) →
⑤ Neonatal H.S ✓
⑥ Eczema Herpeticum ✓
سؤال Pap Smear ← ⑦ Cancer Cervix. ( )
8- Complications of genital (* *)

Q Tzanck smear ?? تتجرب ١٠ ق

Treatment of HSV inf.

Prophylactic

A- For Herpes labialis (HSV1):

1. Avoid triggers e.g UVB —give→ sunscreen.
2. prophylactic Antivirals (before) — حرق بالليزر . / التقشير . / الأسنان .

before 4h / 2w after —
24 hrs before or at morning of the procedure & for 2 Ws after that. (FCV: 250 X 2 / VCV: 500 X 2)

B. For Herpes Genitalis (HSV2):

1. Avoid sex : (the only sure protective Method)
2. Condom use: prevent transmission From ♂ to ♀. ليس العكس
3. Vaccine : Glycoprotein D (HSV2) Vaccine — under trial.
   for prevent of HSV2 in Women That's Sero -ve for HSV1 & HSV2
   [طالما Also : lupidone G & H Vaccines]

(مهم ^ ♀ sero -ve HSV1 & 2)

C- For prevention of Neonatal HSV: (مهم جداً)

1. Cesarean sect : For all cases ē active lesions or prodromal symptoms or ē pH of HSV inf. ← بغض النظر
   - disadv → doesn't prevent inf. Completely " (d.t Transplacental)
     → Expensive.
     → ↑ Morbidity.
2. Recently : (Measures taken if) — the ♂ & ♀ are sero -ve
   — the ♀ sero -ve & ♂ sero +ve
   — ♀ ē Hx of recurrent HSV2

Curative (active) (Episodic tt)

1- Topical
2- Systemic

(NB) ← لازم اسأل عمر إذا HSV

Measures for:

- **Wife:**
  - Avoid Sex in last trimester
  - Vaccine (see above)
  - ACV: suppressive ttt in Last Trimester (at 36 wk)
- **Husband:**
  - Condom
  - ACV: suppressive ttt (during last trimester)

D. Prophylactic chr. suppressive antiviral therapy for recurrent inf. (HSV1 & HSV2):

- indications:
  1. recurrent inf. > 6 outbreaks /y.
  2. recurrent HAEM > 〃 〃 /y. (Herpes ... Erythema multiforme)
  3. physically or emotionally severe outbreaks.
  4. Insufficient prodrome to benifit from Episodic ttt.
  5. Immuno suppression (post transplant)
  6. Suppressive ttt for Sero -ve Couples. (see Neonatal HSV)
  7. ē Kobner phenomena / ē vitiligo
- Dose: → see ttt of H. Genitalis.

NB: → Resiquimod 0.01% gel is

- Topically applied Immune response Modifier used to ↓↓ recurrence.

Resiquimod
Resiquimod 0.01% gel

← قرص أو قرصين (... أو ...) لمدة سنة وأسنوف
أو for life

Active (episodic/curative) treatment of HSV infection

Topical:

1. ACV 5% Cream: (Not) FDA approved
(أدراك) دهان كل ٤ ساعات لمدة أسبوع → علشـ → Rx to syst

2. Penciclovir 1% Cream: FDA approved
دهان كل ٢ ساعتين أثناء عدم النوم (على القطعة اللي فيها) (٤ أيام)

Lipstick 3. Docosanol 10% Cream: FDA approved
دهان ٥ مرات يوميا إلى أن يحدث شفاء.

4. ACV + Topical Cs → Hydrocortisone 1% → (pain) or fluocinolide 0.05%

5. Resiquimode not a gel

Systemic: أول ٤٨ ساعة بس
- ✓ ACV
- ✓ VCV
- ✓ FCV
↓
الجدول

	Type of inf.	Treatment	
1	"Recurrent" H. labiales	ACV (400) → ٥ مرات يوميا لمدة ٥ أيام	[illegible]
	(تشخيص) لأن الأعراض عالية × 1ry H. labialis	VCV: → ٢ جرام مرتين يوميا لمدة يوم	→ تشخيص مريض
		FCV: → ١.٥ جرام جرعة واحدة	→ [illegible]
2	H. Genitalis	→ 1ry attack. → Recurrent "	
3	Neonatal HSV inf.	ACV: (IV) 10 mg/kg (20) every 8 hrs for 10-21 ds (٣ مرات يوميا لمدة ٣ أسابيع)	
4	Immunocompromised VCV 500 FCV 250	ACV → oral: 400 X5 /d or IV: 5mg/kg/8hr (if >12ys) or 10mg/kg/8hr (if <12y) VCV, FCV] ٤ أقراص مرتين في اليوم (durat.) "until all lesions healed"	

NB ACV (IV) → Neonates 10mg/kg/8hr. → Adult & ↓ Imm 5mg/kg/8hr.

(IV) (5-20) → Neonate 20 mg/kg/8hr → <12 ys → 10 mg/kg/8hr → >12y → 5 mg/kg/8hr

• ACV resistent HSV inf. in Immuno-compromised eg HIV	⊙ Foscarnet (IV) 40 mg/kg every 8-12 hr for 2-3 Ws (or until healing) [FDA approved] → not preferred (Nephrotoxic) . Cidofovir 1% (Cream) → (No SE) [CDC approved] or IV Cidofovir 5 mg/kg IV/W X 2 Ws Then EOW.
• Chr. suppressive → in setting of NL individual → in setting of HIV inf.	→ See Genital H. tt & Bolognia.

• General Considerations:-

(A) Guidelines for Antivirals in tt of HSV

(1) should be given during the 1st 48 hrs or during the (prodroma) (tingling, Numbness, Burning) to be effective.

(2) its value is: ↓ pain, ↓ shedding, ↓ Healing time.

(3) Chr. suppressive tt value is:

- ↓ Asymptomatic shedding by ≃ 95%
- ↓ recurrence by ≃ 80-90%

(B) Topical ACV Cream: FDA approved for limited MucoCut inf. in ImmunoCompromised while its use in ImmunoCompetent (may) be (not) effective & may cause (resistence) to systemic ACV

→ على الرغم من ذلك فكثير من الأطباء يستخدمونه

✓ (C) Penciclovir 1% & Docosanol → FDA approved for recurrent H. labialis

(D) Systemic ACV : (not) FDA approved for H. labialis but used by authors / FCV / VCV → approved.

Treatment of Herpes Genitalis

A- 1ry attack → 10 days (7-10)

- ACV (3) قرص ٣ مرات يوميا — or 200 mg X5
- VCV (4) قرص ٤ مرات يوميا
- FCV (3) قرص ٣ مرات يوميا

Tab:
- ACV: 400 mg
- VCV: 500
- FCV: 250

B- Recurrent attack For 5 ds (5-7 d)

- ACV → 3 (as 1ry) — 3
- VCV → 2 tab/d — 2
- FCV → 1 tab/d — 1

C. Chr. suppressive Therapy (> 6 Recurrences/Year)

- ACV
- VCV
- FCV

Start c (2) tab/d for 1 Year & Reasses for frequency & severity.

محافظ على أقل جرعة ممكن أبينه بعد كده

تكمل → For life or Stop after 10 Ys or ACV (6 Ys) & VCV/FCV (1 Y).

طريقة أخرى له:
- < 10/y: ١ قرص يوميا
- > 10/y: ٢ قرص يوميا

ACV oral in children:
- HSV: 15 mg/Kg (Max 400)
- Varicella Z: 20 mg/Kg (Max 800/d).

Varicella (Chicken pox)

- **Def**: primary inf. by VZV usually affecting children.

- **Etiopathogenesis**:
  - VZV (HHV3): • Double stranded DNA
    - • Replicate (intra-nuclear)
    - • produces primary inf. (Varicella) then → latency in Nerve roots —reactivat.→ H. Zoster (2

- **Viral Transmission**:
  1. Inhalat. (main mode) of air borne droplet
  2. Direct Contact c̄ infected vesicles or fluids
  3. Vertical Transmission e.g. Transplacental

(٢١٦) البس جوانتي وانا بدهنله

- Viral inhalat. → inf. of Conjunctiva or Mucosa of URT → replicat. in regional L.N (of URT) → 1ry Viremia on days 4-6th post infect. → replicat. in internal organs (sp. liver & spleen) → 2ry Viremia on days 14-16 post infect. → Viral invasion of epid. & capillary Endothelial cells → Cut. lesions.

- **Epidemiology**:
  - Age: childhood (usually < 10 Ys)
  - Sex: M = F.

- **C/P**:
  - • IP: 2-3 Ws.
  - • Prodromal sympts: usually absent in children & may be (+ve) in adults.

- Lesion has 2 ch:
  - [A] Polymorphic: « all lesions are seen in all stages of Development ».
    (hallmark)

Sequential progression over 12-14 hrs.

. lesion start as: Erythematous macule → Papules → Vesicles → pustule → Crustation & → healing c in (1 W) c̄out scarring

(NB) chic lesion described as:
نزى Dew drop on Rose petal قطرة الندى

distribut = Trunk > Extremities

[B] Centripetal : . starts at Face & scalp

spread: start at the Trunk → extremities (extremities to Trunk)

. oral Mucosa is often involved.

(NB) : the infectivity period: 4 (2) days before Erupt to [4-5 ds] after Erupt (untill all are Crusted).
٤ قبل و ٤ بعد

. Clinical varieties:

(1) Bullous Varicella → DD (BP)

(2) Hgic varicella [usually affect Immuncompromised]
- (Extensive) Erupt of Hgic vesicles.
- High fever & marked Constit. manifs.

. Complications of Varicella :-

(1) 2ry bact. inf → (scarring)

(2) Disseminated inf. → Acute encephalitis, hepatitis

(3) CNS Complication → Reye syn, Guillain Barry syn

(4) Hgic Complications → purpura fulminans [d2 Coagulopathy]

(5) In utero VZV inf.

ⓒ Complications:-

① 2ry bact. inf. by < staph or strept → Impetigo, Cellulitis or Erysipelas → SSSS
خطر [Life threatening].

② Disseminated 1ry Varicella:
. usually seen in → Adults & Immuno Compromised
C/P: → Pneumonitis (rarely < Myocarditis, GN, Hepatitis)

③ CNS Complications: (rare)
- Reye Synd.
- Guillain-Barre synd.
- Acute cerebellar ataxia.

④ Hgic Complications: ← Mechanism Autoimmune
. usually affect Immuno Compromised.
. C/P: [Febrile purpura — Mg. Varicella ē purpura]
[Post infectious " — purpura fulminans]
ⓒ HSP.

⑤ In utero VZV inf. → Transplacental

. Maternal chicken pox → Neonatal affect (1%) w̄ depends on Time of inf.

Period of gestation of infected mother	Outcome in the fetus
7–28 weeks FVS	Fetal varicella syndrome (FVS)
1–28 weeks HZ	Neonatal/childhood herpes zoster
2 weeks before delivery	Neonatal chickenpox
5 days before or after delivery (. 5ds before & 2ds after . 7ds " ")	Neonatal disseminated chickenpox with septicemia and increased mortality (≃30%)

1st 2 Trimest.

. FVS
. HZ
. chicken pox (classical, disseminated)

(IJDVL 2010)

NB. **Neonatal or childhood HZ**: occurs d.t latency of VZV of Mother in dorsal root ganglion → reactivat. later on → (H.Z) c despite (No) History of chicken pox) — حصله جوه الرحم لا يظهر تاني بعد الولادة H.Z

دي حالة الموضوع HZ الع عكسه يعني ظهر ولم يسبقه chicken

- Most Serious Types of Neonatal affect.

(IJDVL 2010) (امتحان) → (A) **Congenital (fetal) Varicella Synd** (FVS):

- Etiology ① usually: Maternal Varicella in 1st - 2nd Trimester (sp. 13th - 20th w)
  أخطر ② less common (10%): d.t Maternal Zoster

  1% of V / 10% of HZ — هل خطورة لو طلعت جراثيم سارية مع الحمل دي عكسه FVS وأكثر شيء يتبعه أقل لو أم جيت لها ch-pox

- Incid: 1-2% of Maternal Varicella cases in (1st - 2nd) trimester.

- C/P:
  - Cut (70%): dermatomal scars.
  - Ocular (65%): Cataract, microphthalmia, Horner synd, Nystagmus
  - Limb hypoplasia (50%):
  - CNS (45%): Seizures, MR (mental retardation), Hydrocephalus, Cortical Atrophy
  - Poor sphincter control (35%)
  - others: LBW.

- Diagnosis:
  ① Amniocentesis
  ② Fetal Blood & Chorionic Villous Sampling
  [isolation of the virus or detect. of sp. IgM]

Neonatal scars ← DD

DD

- Aplasia cutis congenita — ACC
- Epidermolysis bullosa (dominant dystrophic – Bart's syndrome) — EBD
- Neonatal lupus erythematosus — NLE
- Focal dermal hypoplasia syndrome — FDHS
- Antenatal procedures – amniocentesis, forceps delivery, etc.
- Congenital erosive and vesicular dermatosis healing with supple reticulated scarring

(Treatment of Chicken Pox)

- **Prophylactic**
  - قبلها (Preexposure Proph.) → Active Immunizat. (Vaccine)
  - بعدها (Post exp.) → Passive Immunizat. (VZIG)
  - Post exposur. → ACV — بعد 4 أيام من التعرض ولمدة أسبوع (during 2ry Viremia) → "Prevent or Attenuate"
- **Active ttt**

Prophylactic ttt

(A) Varicella Vaccine (USA 1995)

- live attenuated "Oka" strain varicella virus.
- (Indications:) لازم شرطين موجودين
  - Healthy child (not Immunosuppressed)
  - No Past Hx. of Varicella
- 2 doses given at:
  - 12–15 ms (before < 12 less effective)
  - 4–6 ys.
- → routine Immunizat — في دخل الدول

لو مش أخدها عند هذا السن ممكن تعطيه جرعة ثانية عند أي سن

(Catch up Immunizat. of 2nd dose)

- Efficacy · (90%) → prevent inf. (100%) → protect against mod. severe inf.
- this efficacy (↓↓) ē Time (84% after 8 ys)

(+) · NB: Break-through dis. involves varicella that occur after 42 ds. of Immunizat⁻ when it occurs called Modified Varicella like synd⁻ ω is similar to varicella but milder & ch⁻ By:

- Milder Constit. manif.
- NO of lesions < 50 vesicles.
- Papular lesions are common.

(مش هي Recurrent varicella)

Passive Immunizat⁻ (VZIGs)

⊙ Indicat⁻ : (..ac L (97) ...)

Post exposure (in 2 situat⁻) · Immuno Comp. · Mother — Neonates

1. Post exposure prophylaxis of Immuno Compromised
2. " " " " pregnant ♀
3. Neonate if ! mother acquire infect⁻ 5 ds before or 5 ds after (or 2 ds) delivery.

VZIG is administered intramuscularly, never intravenously. The dose is 125 U/10 kg body weight; 125 U is the minimum dose. Maximum dose is 625 IU. Administration as soon as possible after exposure is best, but VZIG can prevent or attenuate varicella if administered within 96 hours of contact. The expected duration of protection is approximately 3 weeks.

Intravenous immunoglobulin (IVIG) has been used to prevent varicella after exposure when VZIG is not available. Clinical efficacy is not exactly known. Patients already on replacement IVIG do not need VZIG if their most recent IVIG infusion was within 3 weeks.

⊙ Efficacy: ↓ Mortality & Complications (Not) the incid.)

VZIG does prevent inf. ?? Prevent or Attenuate but ↓ MoR & Complicat⁻ ← اجابة ...

Active ttt

(1) Symptomatic ttt:

- Antihistamines
- Topical Antipruritic
- Antipyretics → ممنوع أسبرين للطفل
  - ↓ (<6%) children ē viral inf. may → **Reye synd** (Acute encephalo hepatitis)
  - Diagnosis: Varicella + severe vomiting + lost consciousness.
- Antibiotics

(2) Systemic Antivirals: (ACV)

لازم ٢ خلال ٢٤ ساعة برضه (or 24-72)

varcilla → علاج ٥ أيام

H.Z → ٧ أيام

Non approved Indications (Controversy)

Healthy child ≤12 ys (or 40 kg) ē (Un)complicated Varicella.

(1) رأيين: مفيش داعي نعطيه لأنه هايخف لوحده بس مع غيرت كل والعلاج تأثيره بسيط

(2) نعطيه بشرط: المريض يقدر يدفع Cost لو جالك في أول ٢٤ ساعة

- مع علاج ال Chicken ← ٥ أيام أو جرعة ٤ مرات
- " " Zoster ← ٧ أيام أو الجرعة ٥ مرات

ACV: 20 mg/Kg/dose (max: 800 mg) (4) times/day for 5 ds.

VCV (FDA [illegible] حديثاً): 20 mg/Kg/dose (max 1gm) (3) times/d for 5 ds

approved Indications

([illegible])

1. child >12 ys or >40 kg
2. child <12, healthy ē Complicated Varicella (pneumonia)
3. pregnant (oral)
4. Neonatal (IV)
5. Immunocompromised (IV)

→ 10 mg/Kg/8hr IV [drip over 1hr] for 7-10 ds

Herpes Zoster
(shingles)

Def: Acute condition ch. BY appearance of Grouped Vesicles along the course of a Nerve.

AET: • Reactivation of Latent VZV in dorsal Root ganglion.

- 1ry inf. by VZV → [chicken pox] → laten in post. Nerve Root & ganglion → (Reactivation) → [H.Z]
  ??

• **Ppt. Factors:** Reactivation May occur Spontaneously but may be precipitated by certain factors:

- Immuno suppression. e.g Leuk., Lymphoma, Cs, HIV
- Drugs
- physical trauma عملية منه
- Stress
- Radiation

(صدفة)

- Ext. exposure to virus.
  [راجل عجوز دخل عنده جديري أو صاحبه عنده (HZ)

  لو اتعرض لـ chicken pox أو HZ

Age: elderly (>60)
Sex: M=F

Clinical picture

[Pain] → (1-10 ds) (≃ 48 hrs) → [Eruption & Manifs] → >4 ws → [PHN] (Post Herpetic Neuralgia)

Pain:
- Called Acute Zoster pain (Prodromal pain)
- usually before eruption by (1-10 ds)
- May be absent & 1st presentation is the Eruption.

[Severity] depend on:
- Age
- severity of eruption
- Immune Compromized.

Eruption & Manifs:
- allong the affected Sensory or Motor or Cranial Nerve.
- Erythematous papules & plaques $\bar{c}$ in hrs → Vesicles (Multiple grouped Vesicles on erythematous Base).

Pain (Prodromal & Acute Zoster pain)

- Acute Zoster غالبا نوع الألم
- "PHN" هو نفسه نوع الألم

٣ أشكال:
- Continuous burning or dull aching — ضاغط كسرة
- Spasmodic shooting (Neurotic) — لسعة كهربا
- Triggered
  - Allodynia (non painful stimuli as touch → causes pain) مع لبس الهدوم
  - Hyperalgesia → (mild painful stimuli) → (severe pain)

✓ [dermatomal, unilat

> • Pain before Eruption may be Misdiagnosed as:
> - Migraine
> - MI
> - Pleurisy
> - Acute Abdomen

Eruption → Common affected dermatomes (بالترتيب)
- Thoracic
- Cervical
- Facial (cranial)
- Lumbosacral

> Zoster related pain may be classified as:
> 1. Prodromal pain (before Erupt.)
> 2. Acute Zoster pain (ass. c̄ Erupt.)
> 3. PHN.

- Eruption may remain to develop over the Next **1-7 ds** (ACV ضروري تعطيه في هذه الفترة)
- strictly unilat (Not crossing the middle lines except in severe cases & immunocompromised)
- Healing within **2-3 ws** (in healthy patients) or upto 6 ws (In immunocompromised) usually by a scar

Manifestations [Zoster mainly sensory]

① Motor Manifestations: (5%)

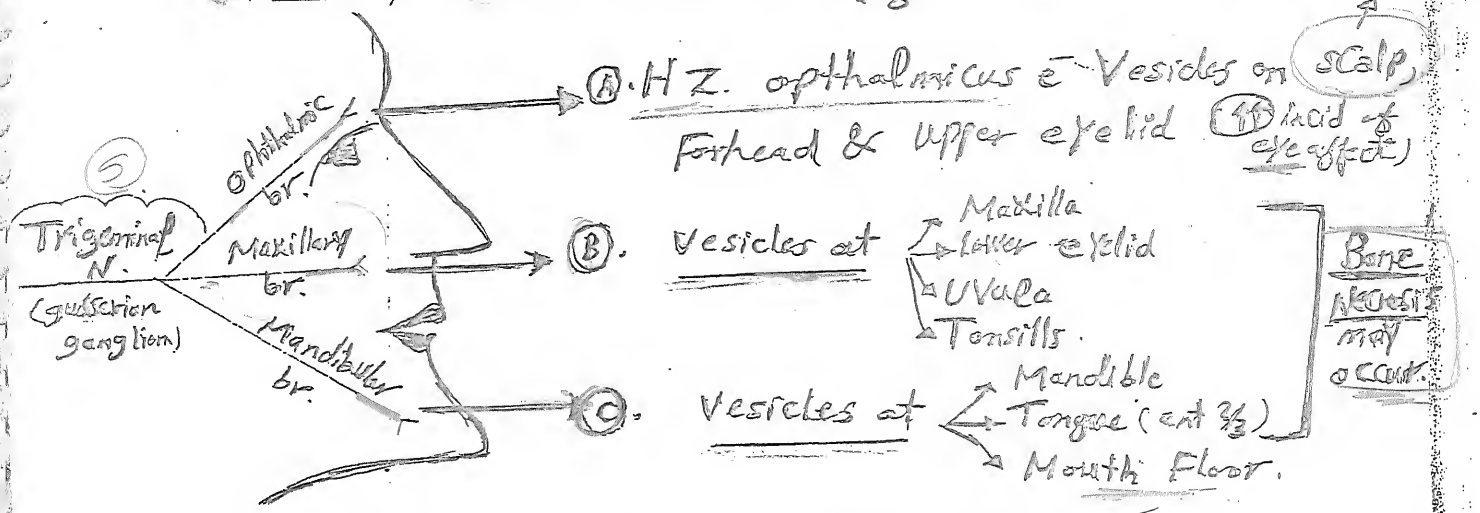
[Rarely Reversable]
- Facial palsy (7th)
- Ocular paralysis (5th)
- Abd. Hernia (Tho. LII) → abd. ms paralysis
- S2, ③, 4 → urine retention, hematuria, dyschezia & Pseudo obst.

②. Sensory manifs:

أشهر

(HZO) : H Z ophthalmicus → Headache like pain (Migraine).
: N Thoracic → pleurisy or MI like pain.
: N Abd. → Acute Abdomen like.

(5) Cranial Nerve affection :- (5) / (7) / (8) → * Trigeminal



* (7) th. Cranial (Facial Nerve) [Reactivation of virus at Geniculate ganglion or dorsal Root]

Facial N. paralysis is Complete & Recovery only in (2)%

(1) at First Sensory fibers involvement → HZ Oticus
(Vestigial by)
e.g. Otalgia
Vesicles at ext. auditory Canal & Pinna

(2) Pressure at Motor fibers → Ramsay Hunt Synd
[Soft palat Tonsillar fossa]

then ±

(3) Otalgia
Vesicles at Ext. and Canal
facial palsy (±)

(4) Pressure on (8) th N. or direct Transmission of Virus (at MPA) ear
Vertigo
dizziness
hearing loss

(3) Pressure on Intermediate N. (or its Geniculate Ganglion) (br. from 7th.)
X loss of taste from ant 2/3 of Tongue (±)
[lacrimal gland affection.

[So, Ramsay Hunt synd is ← & usually as (e)]

NB

(ازاي) ... Eye affection in H·Z

HZ ophthalmicus (HZO) with vesicles on upper eyelid. → Gasserian gang. of Trigem. N.

(Zoster ophthalmicus ... C Rumsay)

⊙ Eye affection by H·Z — لازم نعمل ٣ حاجات
- IV ACV
- systemic Cs
- ophthalmologist (in ophth.) or ENT in (facial palsy)
- Consider: Meningitis.

Hutchinson's sign — Vesicles on tip & side of Nose if the ext division of Nasociliary br. (br. from ophthalmic supplies cornea) is involved

↓

. When the sign ??
- +ve → 75% affection
- -ve → 25% "

. Forms of ocular involvement:
- Uveitis (90%)
- Keratitis (50%)
- ocular paralysis.
- Iridocyclitis
- glucoma
- Acute Retinal Necrosis.
- ArgYL Robertson pupil

مهم

سؤال: مريض جاله H·Z ophthalmicus وبعد شهر ونص (بعد ما خف) جاله facial palsy or Hemiparesis → "Explain"

↓

. the Trigeminal (specially ophthalmic) has intracranial branches → extension of infection from the extracranial brs. to intracranial brs → CNS affection & Cerebral arteries thrombosis → Hemi-paresis & Headache.

. Ttt: (systemic AntiViral)

Clinical Varieties of HZ

[illegible]

1. Classical type (Vesicular)
2. Bullous (Bullae on erythematous base)
3. Abortive (Zoster Sine herpete): (No) vesicles or Bullae; only pain &/or Erythema. = (ما بيكملش) بيروح للأنسجة بتاعة الـ nerves
4. Haemorrhagic
5. Gangrenous (Necrotic).
6. Generalized = disseminated = Zoster Varicelliform (امتحان) — > 25 extra dermatomal lesions occur 1-2 wk after 1ry Erupt. — imp. مهم
7. Ecthymatous (Punched out ulcer) — Ecthyma [illegible]
8. Verrucous

(7, 8 →) HIV — immune-Compromised = (bad prognosis)

Post Herpetic Neuralgia (PHN) — imp. مهم

< 60y → 15%
60y → 50%
70y → 75%
] — PHN

2 definitions:
- Persistence or Recurrence of pain For > 1m from onset of Zoster (e.g Rook)
- pain that start or persist after healing of Rash.

incidence ↑↑ ē:
1. ↑ age (age > 50 is of higher Risk)
2. Immune Compromised
3. Severe H.Z.
4. H.ZO or Ramsay Hunt

ttt of H.Z → prophylactic ttt / active ttt

ttt of Acute Zoster

- **Instructions**
  1. راحة في السرير
  2. كمادات ماء (ساخن) (زجاجة ماء دافئ)
  3. Abd. binder → يوضع قطن على مكانه ويلف برباط ضاغط
- **Topical ttt**
- **Systemic ttt**
  - Systemic antivirals
  - " Cs
  - Analgesics

ttt of PHN

- prevention
- Active ttt
  - Topical ttt
  - Systemic ttt

Prophylaxis of Zoster

Vaccine : ذ شرط Good Imm.

(LAV) [Zostavax]

→ Live attenuated Vaccines (ZostaVax) in 2005 (For) pt. ē good Immunity.

- CDC (2006) → recommended it For any pt (≥ 60 Ys) even those ē previous Zoster.
- FDA (3/2011) → (50-59 Ys.)

• duration of protection ??

⊙ In general indicated in:

1. Any pt > 60.
2. Any pt ≥ 60 going to have Biological therapy e.g (Ps, RA)
3. (WIKI) boosting dose may be given in pts > 60 ys exposed to child ē chicken. [post exposure prophylaxis].

⊙ Contra indication: XX → (Immuno-suppression. e.g Cs, chemo or radiation. ✓

Varicella-Zoster Igs

خطر : Immunocomp exposed.

↓

• protect against Varicella & Zoster for (≃ 3 ws.)

• [CDC] indication: (>60) pt. who is susceptible or Immunocompromised & exposed to Varicella or Zoster

ويفضل الإعطاء مبكراً بعد التعرض للعدوى مباشرة (لحد ٩٦ ساعة من التعرض) (مش بيبقى فعال)

• [Value]: prevention or modification of dis.

· Topical ttt

Vesicular lesion → ① drying antiseptic lot
- Burow's sol (Alum. Acetate)
- Tr. Benzoin & Flexible Collodion (1:1)
- Alcohol + Menthol + phenol. [Calamine]

② Acyclovir cream (٥ مرات يومياً)

Crusting lesion → Antibiotic → Topical / Systemic

Systemic ttt → Antivirals. / Cs. / analgesics.

① Systemic Antiviral

Value:
- ↓ duration of disease course,
- ↓ pain
- ↓ incid of PHN.
- ↓ New lesion formation.

NB: In Immuno competent the efficacy of ttt beyond 3-4ds (or 48hr) is unknown

indications:
1. All immune-compromised
2. pts > 50 ys (↑ incid of PHN)
3. HZ ophthalmicus (HZO)
4. Ramsay Hunt synd
5. severe disease or severe pain
6. (Cut) Visceral or Motor affection. dissiminated.

(NB) - Young cases ē mild affection → No need for systemic Antivi.
- the benefit of Antiviral if given after 3-4ds in Immuno competent unknown
- in severe cases: we may need to start IV

. ACV (tab = 800) قرص ٨٠٠ مجم ٥ مرات يومياً
. VCV (tab = 500) قرص (١٠٠٠ مجم) ٣ مرات يومياً
. FCV (tab = 250) قرص (٥٠٠ مجم) ٣ مرات (7 days)

Potency: FCV > VCV > ACV

(لازم خلال ٧٢ ساعة)

← يفضل بدأ العلاج في أول ٧٢ ساعة
← لكن لو كان عدى ٧٢ ساعة ولازال الطفح بيظهر جديد أو كان المريض Immuno suppressed ممكن تعطى لحد أسبوع من ظهور الطفح -

. Indication of (IV) Antiviral :-

1. immunosuppressed ē → ophthalamic Zoster ✓ → Ramsey Hunt Synd. ✓ → dissimination ✓
2. Faild oral therapy.
3. HZ ophthalmicus (HZO)

dose: 10 mg / kg / d 3 times / day for 7 ds. (IV over 1hr ??)

. in elderly patient ē unknown Renal state
↓
start ē FCV or VCV (2 times / d) till assessment of Renal condition
or
use ACV from the start

Creatine clearance اقل

(HL)

. for patients ē RF (creatinine clearance of < 25 ml / min)
↓
اقل الجرعة بتاعته

ACV is prefered.

(2) Systemic Corticosteriods

Value جدل في صحته
→ ↓ Pulm oedema & inflamm. → ↓ Acute Zoster Pain
→ Rapid return of patient to his activity.
→ ↓ incid. of PHN (controversy)

(شروطه)
→ should be within the 1st week
→ 40-60 mg / d for 1 w then withdraw over 3-4 ws
→ avoid it : in immunocompromised
→ under cover of systemic Antiviral

40
4

: Mechanism : (↓) the perineural inflamm. & oedema so ↓↓ fibrosis.

(3) NSAIDs / or opoid agonist (Tramadol).

PHN

[difficult to be prevented & treated].

(Prevention)

- Antiviral (Early ttt) → [VCV > ACV]
- Syst. Corticosteriods (Controversy)
- Amitryptaline (25 – 100 mg/d)
  (Tryptizol 25 tab ... ال ٤ أقراص بالتدريج)

Amitryptaline (Tryptizole 25mg tabs)

Treatment

Topical

- Capsicum (Capsiocin 0.025% & 0.075%) ®
- Lidocaine 2.5% C
- prilocain (EMLA) ®
- Topical Aspirine
- Intralesion corticosteriods (0.2 mg/ml Intralesional or S.C)
- Intralesion Cs + Procaine
- Nerve block & Pain clinic Referral.
- ACU Puncture

Systemic

Table 2 Treatment options for postherpetic neuralgia

Drug class	Examples	Initial daily dose (mg)	Titration to maximum dose
Anticonvulsants	Gabapentin	100–300	Start qhs and increase to tid dosing; increase by 100–300 mg every 3 days to total dose of 1800–2400 mg/day
	Pregabalin	150	Titrate up to 300 or 600 mg/day
Opioids	Tramadol		
	Hydrocodone	5–10	No titration
	Oxycodone (extended-release)	20	Titrate up to 60 mg daily
Tricyclic antidepressants (TCA)	Nortriptyline	10–25	Increase by 10–25 mg weekly with a target dose of 75–150 mg
	Amitriptyline	10–25	
	Desipramine	10–25	

Tegretol ... TEN ...

- Some authors recommend: Combination bet. Tryptizole 25mg + Tegretol 600–800 mg (Effective). (Carbamazepine).

Antivirals Against Human Herpes Viruses

Classificat°

Topical

- ACV
- PCV
- Docosanol

→ أهمّ (Pencyclovir)

- Cidofavir
- Foscarnet

→ under trials

Systemic

٣ أساسيين
- ACV
- VCV
- FCV

جديدين
- Cidofavir
- Foscarnet

- Ganciclovir
- ValGanCiclovir

- ACV (Acyclovir, Aciclovir)
- VCV (Vala ~, Vala-~)
- FCV (Fam ~, Fam ~)

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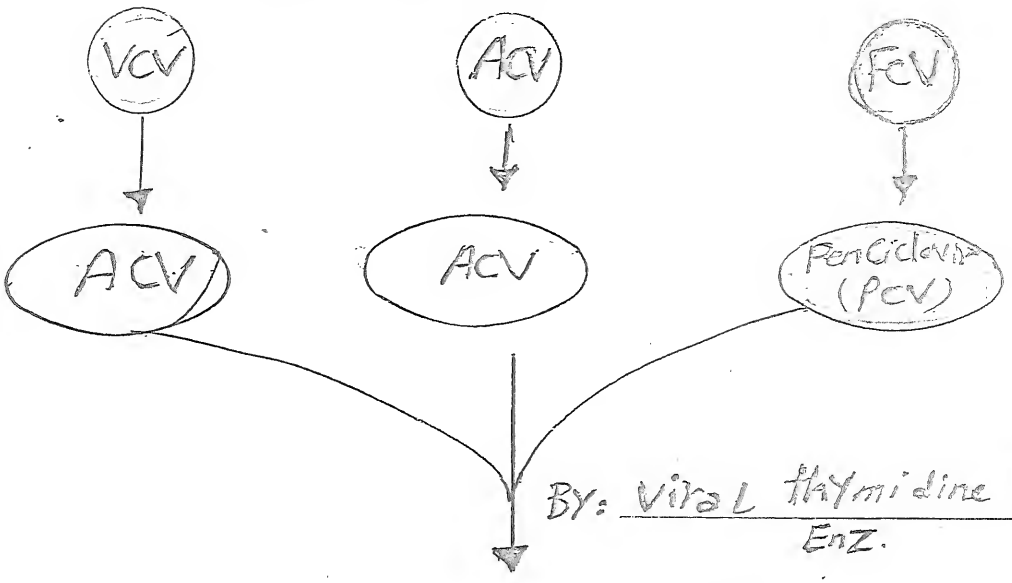
1. Mechanism
2. pharmacokinetics
3. Indications
4. C.I
5. Dose
6. S.E
7. interactions.

Mechanism



BY: Viral thymidine Kinase Enz.

ACV or PCV (Mono-) Phosphate

BY: Cellular thymidine Kinase Enz.

ACV or PCV (Tri-) phosphate

Concentrate inside infected Cells (40 times > NL Cells)

Competitive inhibition of GTP For Viral DNA polymerase.

Stop Viral DNA Elongat=

(Chain Terminat=)

B.

VCV: Prodrug of ACV

FCV: " of PCV.

خطوات

1- Activat= : to Monophosphate form

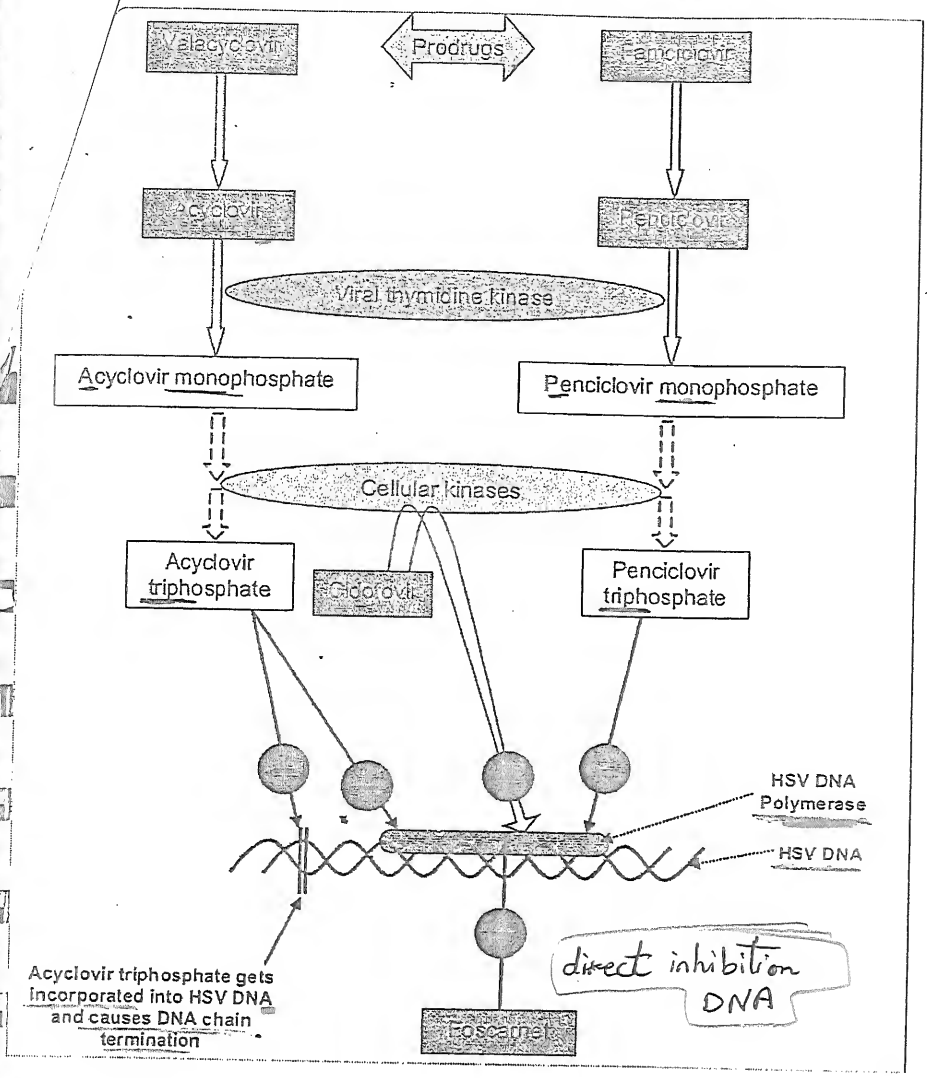
2- Accumulat= : inside infected Cells

3- Inhibition : of DNA polymerase

4- Chain Terminat= : -- DNA Elongat=

of Dermatology, and Leprology

Figure 1 :Major mechanisms of action of anti-herpes simplex virus antiviral drugs



%

Doses : (see HSV & VZV) . يحفظ جيداً

S.E : • ACV usually safe but S.E may occurs at the following:

1. IV route
2. Bollous dose (if not given by IV drip over 1 hr)
3. Large doses for longer durations.

• SE may include:

٣ عاديه
1- Headache & Cough
2- Rhinitis
3- Nausea & diarrhea.

٣ مهم
4- phlebitis (at site of IV).
5- Obstructive (crystalline) Nephropathy [if given rapid not by IV drip over 1hr, < 10 min] — Reversible (خطيط)
6- Resistance. (مهم جداً)

شفوي Q
(HIV مريض، HZ or Hs لو جاله تعالجه ازاي ؟؟) → in (HIV) patients due to Mutat. in HSV → No viral Thymidine Kinase → No activat.

↓ الحل ← ؟

Viral thymidine Kinase ?? نحط حاجات لا تعتمد على

« Cidofovir & foscarnet » → direct DNA --

↳ Cellular CK

Interactions : نادرة ليه ؟؟

↓

because it's not Metabolized by Hepatic Microsomal enzymes (CYP-450). (cytochrome P450)

(احفظ كتابته بالجدول)

Categorizat. : Pregnancy category (B)

دي هتفرق الحمل
داخيا لازم نحفظ

Vala Cyclovir

- def. L-valyl esterase of
- Mechanism: VCV $\xrightarrow[\text{By valacyclovir Hydrolase}]{\text{hepatic \& intestinal (first pass)}}$ prodrug of ACV.
  ACV + L-Valin (a a

- Differs from ACV in:

↑ (1). Bioavailability: (≃ 60%) (≃ 3 – 5 Times as ... ACV: So
→ efficacy of oral VCV = IV ACV
→ lower doses are Needed (< ACV)

✗ (2). Not approved For chicken pox

↑ (3) More effective in Ameliorating PHN > ACV.

(4) Dose: HSV → labialis → (Episodic 4 gm/d)
→ Genitalis → (" : 2X500X5-10)

HZ (500X3X7)

Suppression
→ <10
→ >10

Fam Cyclovir

(Famvir; 125, 250, 500) (R)

very similar to VCV → but differs in:

→ Prodrug of penciclovir.
→ Bioavailability → 75%
→ efficacy = VCV & ACV.

Current FDA-approved antiviral drugs (excluding antiretroviral agents)*

HSV / VZV

- Acyclovir (Zovirax®) ACV
- Famciclovir (Famvir®) FCV
- Penciclovir (Denavir®) PCV
- Foscarnet (Foscavir®)
- Valacyclovir (Valtrex®) VCV
- Trifluridine (Viroptic®)
- Vidarabine (Vira-A®)
- n-Docosanol (Abreva®)

CMV

- Ganciclovir (Cytovene®, Vitrasert®). GCV
- Valgancyclovir (Valcyte®). VGV
- Foscarnet (Foscavir®).
- Cidofovir (Vistide®).
- Fomivirsen (Vitravene®).

HHV-8

- IFN-alpha (Intron A®, Referon A®).

HPV

- IFN-alpha (Alferon N®, Intron A®).
- Imiquimod (Aldara®).

VGV

Hepatitis B virus

- IFN-alpha (Infron A®).
- Lamivudine (Epivir-HBV®).

Hepatitis C virus

- IFN-alpha (Intron-A®, Roferon-A®).
- Peg IFN-alpha (Peg Intron®).
- IFN-alpha + Ribavirin (Rebetron®).

Respiratory syncytial virus

- Rivairin (Virazole®).

Influenza virus

- Amantadine (Symmetrel®).
- Rimantadine (Flumadine®).
- Zanamivir (Relenza®).
- Oseltamivir (Tamiflu®).

* J Am Acad Dermatol. 2002. 47. 581-99.

• HPV Virology

- Papovirus Family
- Diameter: 52-55 μ.
- Naked; No evelop
- Capsid → 2 proteins → Major capsid protein L1 (95%) / Minor " " (5%)
- Reservior of it → Basal KG.
- Incid: infect 10% of Populat; sp. 12-16 Ys.
- Transmission → جنسي

• Host Immune Response

"How HPV evade the Immune System"

1. No Viremia
2. low levels are expressed at KCs → Basal / st. Malpighii — to be recognized by LCs & Infilt. lymphocytes.
3. Upper layers (differentiated) → Extensive virion protein product → shedding ē epith.

• Role of Immune Surveillance ?? مراقبة

→ • 60% of warts regress ē in 2 Ys.

- ↑ Incid. in pt. ē ↓ CMI.

→ Antibodies against HP 16 detected in 50% of Women ē asympt. or low grade Inf.

هل لم لها علاقة تحدث من جدوش

عدوى بنفس النوع أو من الطرف الآخر (sex. Partner)

Warts (Verrucae)

Def. Benign Epid. proliferations (Tms) caused by Human papilloma virus (HPV) inf. of ē skin & MM

. HPV belongs to Papovirus group ŵ are:

- slowly growing
- double stranded DNA; Replicate intranucl.
- Naked (no envelope; so resist (freezing, drying, solvents))
- > 100 types of HPVs discovered.

. Mode of Transmission:

1. Contact
   - Direct e.g. الإمساك باليد
   - indirect e.g. الملابس
   - autoinoculation. (causes → local spread.) e.g. بينقلها لنفسه
2. Sexually transmitted.
3. Vertical: Perinatal during vaginal delivery. ✓ أولادها قيصري

. Types of infection:

① clinical: lesions seen by Gross inspection.

② subclinical: lesions seen (only) by aided exam. (acetic acid soaking).

③ Latent: - presence of HPV virus or viral genome in apparently NL skin.

. Thought to be common specially in Genital Warts & Explains in part the failure of destructive methods to Eradicate Warts.

Why Recurrence is Common → ليه

. Epidemiology:

- incid. of inf.: (10%) of children & young adults
- Peak age incid.: 12 - 16 ys.
- I.P: Variable; range from 1-6 ms (in common Warts)

HPV Classification

- **According to Risk of Mg Transformation**
  - * Non Risky group: 1-4 types
  - * Low Risk group: 6, 11 types
  - * High Risk: usually: 16, 18 / 31, 33 / 45
- **According to Type of infection** → (See below)

استثناء

- Verrucous SCC : HPV6
- HPV 5 & 8 : EDV

احفظ كويس جدا

- 6 & 11 : Low risk
- 16, 18, 31, 33, 45 : High Risk

HPV Infection : "مهم"

Genital

- **High Risk HPV (16, 18)**
  - * Bowen's dis
  - * Bowenoid papulosis
  - * High grade intraepithelial Neoplasia.
- **Low Risk HPV (6, 11)**
  - * Genital Warts
  - * Low grade intraepithelial Neoplasia. (CIN)

⊕ Buschke & Lowenstein Tm (HPV6 استثناء)
⊙ Digital SCC (rare).

Non genital

- **Cutaneous**
  1. Cut warts.
  2. EDV
- **Mucosal**
  1. Laryngeal < Papillomatosis / Cancer
  2. Conjunctival <
  3. oral
     - Papillomatosis
     - Cancer
     - Leukoplakia
     - Heck's dis (13, 24, 38)

NB

- كل نوع من الفيروس بيفضل مكان معين للعدوى.
- عكس النوع الواحد يعمل عدوى في اماكن مختلفة

سؤال شفوي (Common ⇌ Genital)

- ↑ ~~Expression of Viral E6 & E7 & Protein E2~~
  المسئول → (oncogenicity)

Discussion of Non genital HPV inf.

1. Cut. Warts
2. EDV
3. Heck's dis.
4. Laryngeal papillomatosis

Cut. Warts: (Verrucae)

- Types:

Types	HPV type
1- Common (Verruca Vulgaris)	2, 4
2- Planter (Verruca plantaris) — أنواعه	Mosiac: 2, 4; Myrmecia: 1; Cystic: 60
3- Flat (Plane Wart; Verruca plana)	3, 10, 128
4- Filiform (Digitiform)	as Common Wart 2, 4
5. Butchers	7

NB* Verruca (لازم) → Growth Rough

- Description:

1. Common Wart: (Verruca Vulgaris):

- site: any site but
  - Commonest: Hands (finger, Palms) & Knees.
  - in Nail biters: → Lip & Tonge.
  - Butchers: on hand; caused by specific HPV which is Type (7) (Not a bovine but Noted to associate butchers). → (الجزارين) extensive exophytic or Cauliflower lesions.

in Nailbiters
Wart ± affect: periungual, Lip & Tongue

- shape: Flesh Colored papules → dome shapped (gray to brown) Hyper Keratotic discrete & Rough Papules

3 NB.s

- Black Color (dots): represent thrombosed BVs.
- On paring using blade: Prominent Capillaries (كحت بالشفرة) & ± Bleeding.
- Warts show interruption of dermatoglyphics (finger prints). XX مش موجودة

• prognosis: 65% shows spont Resolution within 2 Years.

• All Warts are painless Except: planter wart.

HPV 2, 4 ← • Filiform = digitate wart: long, slender growths seen on Face around lips, eyelids & Nares.

* Flat, plane, or Juvenile warts: (3, 10, 28)
  * Flat topped papules that are slightly erythematous or brown on pale skin & Hyper pigmented on darker skin.
  → usually multiple
  - Site: Face, Neck, dorsa of hands, Elbows & Knee

NB
- auto inoculat^n عكس تحرشة ← الرجال: اثناء الحلاقة الذقن / الاناث: ازالة الشعر الرجل
- May show pseudo-Koebner phenomenon (linear flat topped papules).

• HP of cut warts:
1. Hyperkeratosis
2. Parakeratosis
3. Acanthosis
4. Papillomatosis
5. Vacuolizat^n of Horny cells
6. Koilocytosis (below granular layer) ← EDV على
7. Inclusion bodies
   • Basophilic: AbNL KH granules
   • Eosinophilic: Viral Particles
8. Edematous Cell & Tortuous Capillaries

NB. Plane wart (Not) marked Hyperk.

• Plantar Warts = 4 types (5) Plantar epidermoid cyst

1. Mosiac Warts
- plaque of closely grouped Warts
- When Pared: angular outline of closely compressed individual Warts can be seen.
- site: Sole (± palm)

2. Myrmecia (Deep)
Smooth, deep, dome shapped, tender (±) inflammed papule emarked protrusion beneath the skin → Very painful
- site: sole & hands (digits & periungual).
- pressure sites: Heel & metatarsal head.

3. Ridged
non weight Bearing areas preserved skin lines (dermatoglyphics)

4. Cystic
Smooth Cystic nodule on weight bearing areas
- incision → cheesy material

2, 4 HPV

• HPV 1

HPV 60

• Heck's dis. (Focal Epithelial Hyperplasia):
- HPV inf. of oral cavity: 13, 24 & 32.
- Multiple flat topped (or) dome shapped "pink-white" papules affecting oral cavity (specially: Lower lip). ← Q

Tt: Cryo, Laser, surgery, IL IFN

DD: Cowden Syn. ←

Characteristic Unit 12

EDV

2014 (1)

Epidermodysplasia Verruciformis

(2012) (2014) (6)

لوحيت تأخذها جزءا
بيجي ده كتير

1- AR (but ± Sporadic, AD, Sex linked)
2- HPV 5 & 8 (also other types)
3- plane wart like lesions
4- TVC like lesions
5- SCC (20-40 ys)

(اوعاها)

→ **Def** → rare inherited (AR) disorder ch̄ BY wide spread HPV inf. & SCCs

HPV (>30) → Specific types (5, 8 & 47) (9, 12, 14, 15, 17, 19, 25, 36-38)
→ other Types (non specific) : 3 & 10.

Etiopathogenesis (Triad):
1- Genetic defect: Ever 1 & EVER 2 → Immunosuppression.
2- HPV (see above)
3- UVB : Immunosuppressive & Mutagenic.

Clinically:
- 1 & 2 → at childhood (± Cong)
- 3 → at Adulthood.

Plane wart like Lesions
- but more extensive & Flat.
- At: Face & Neck, dorsal Hands & feet (sun exposed)

NB (3) → Plane Wart like, Pigmented plaques, Dysplastic changes (AK, Bowen's, SCC).

TVC like Lesions
- Scaly Hypo- or Hyper-pigm. macules

SK like Plaques
- Large Verrucous Pink-Violaceous plaq.

(TVC & SK like: Trunk & proximal limbs.)

3 SCC (UV induced) (اوعاها)
Can affect any area of Body but more Common on sun exposed areas
affect 30-60% of Cases bet. the age bet. 20-40 ys.

مفيش علاج
مجرد كام علاج من ضمنهم شيء بيولوجيا

Rx
1. Avoid sun (to avoid SCC)
2. Surgical Rx
3. Retinoids (≠ SCC)
3 5 FU, Imiquimode, IFN

DD :-
1. Acrokeratosis Verruciformis of Hopf :
   - Infant ē : Extensive plane wart like lesion at Hands, feet, Elbow & Knee + PP Keratosis.
   - HP → No vacuolization
2. Generalized Verrucosis in HIV, LL, Lymphoma

• Pathology: "specific": upper Epidermal Cells have Clear, smoky or light blue Cytoplasm & Central Pyknotic Nucleus, + (Hyperk + Acanthosis ± Dysplasia)

(Clear Cells) (Vacuolizat)

• Insitu hybridizat → detect DNA of HPV in KCs.

Recurrent Laryngeal papillomatosis Q مهم

(تاتی RT) → • Recurrent Respiratory (nose → lung) papillomatosis may have 2 age groups:

• Age < 5 → usually acquired from the mother (during vaginal delivery) who having Condylomata ACC. So the HPV is of 6 & 11 types. (من الأم)

→ • Triad of — Hoarseness — stridor — RTD

• Fatal Carcinoma.

• Age > 5 → Acquired by other Routes as plume of "رذاذ" Laser or Electrocautery → (الأطباء يحصل لهم أثناء الكي)

So → All pregnant ē Condylomata should undergo Cesarean sec, (سؤال شفوي) (despite some infants born by C.section showed laryngeal papillomatosis) نادر

NB

HPV in Immuno suppressed

- organ Transplantation
- Immunosuppressive medications
- Cong. Immuno deficiency
- Lymphoma
- HIV

— all → defective (CMI) → ↑ susceptability of HPV inf.

- Incid ↑
- Type
- distribut & site
- ↑ Dysplasia
- Ⅲ cap

C/P ① Wide Spread: → Generalized Verrucosis (EDV like)
② ↑ Incidence of Dysplasia ③ Resistant to Ⅲ

• HIV & HPV

(i). Warty Keratoses at angles (often Bilat) chic & unique, caused usually by HPV (2, 27 & 57.)

(ii). ↑ incid. of Genital warts → (15 fold).

(iii). ↑ incid. of Cancer → HPV 16 & 18

• D.D of Cut wart:

Callosities
- ①. Callus
- ②. Corn (clavus).

③. Black Heel

④ Pitted Keratolysis

• Callus — "non penetrating"

"diffuse" Hyper Keratotic areas d.t chr. Repeated → Friction / → pressure (ill defined)

أماكنه
- Sole · under 1st & 5th metatarsal head
- Palm: العمال
- dorsum of Hand: MCP & IPJ in Bulimia individuals.
- dorsum of feet: علامة الصلاة

→ Asymptomatic or painful on pressure.

"penetrating" • Corn

Conical shapped Hyper Keratotic area thats well defined & d.t pressure, Friction or shearing forces of bone against adjacent digits, metatarsal heads or footwear

- • Poorly fitting shoes most common cause.

غالبا بيصبح بروز عظمي ← غير طبيعي

has 2 types

Hard Corn (حمة كالبشكال)
↓
• dorsolat aspect of fifth Toe.

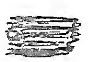
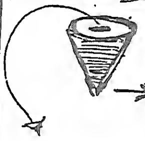
Soft Corn
↓
بين الصبعين الرابع والخامس للقدم (site of T. pedis)

may be d.t
- Friction of Bone of 2 Toes
- maceration

↓

- usually misdiagnosed as T. pedis.
- may produce sinus tract in the web → Recurrent bact. & Fungal infection.

B Pain: dull discomfort or knife like

Callus	Corn
 "diffuse Hyperkeratosis"	 → on the surface; → deep in skin; (Nucleus or Central Core) "Conical Hyperkeratosis"

• صوابع القدم الصغير (dorsolat. aspect)
↓
painful lesion
↓
Corn (usually Bilat.)

بين صوابع الصغير واللي قبله
↓
thickened painful area → soft corn

وخلي بالك تفرق بينه وبين التينيا

السؤال المحتم ؟؟

Q: How to differentiate bet. Wart (planter), Callus & Corn

- See Skin lines (dermatoglyphics)
  - Continous over the lesion ē No central Core) → Callus
  - Interrupted over the lesion with central Nucleus (Core).
    - Wart or
    - Corn
    - ↓ إكحت بالمشرط (Paring off.)
      - **Wart.**
        - Markings always lost
        - (Ip.Y) → Bleeding
      - **Corn**
        - markings first lost over the central Core but ē Continous paring → appears again.
        - No Bleeding. [Small toe]

وماتتساش الأماكن المميزة

- **Treatment of Callus & Corn:**

1- ℞ of the cause: → Soft wears (كوتش) → Correction of any bony abnormolities (Bony prominence)

2. See saliclic acid ℞ of wart.

3. Intra lesional Cs → dramatic Relief of pain in Corns.

→ Cancer.

"HPV of Genitalia"

Classified into

- **Low Risk or Benign types.**
  - ≃12 types of HPV
  - Commonest [6 & 11] (6: 25% > 11: 25%)
  - ① Condylomata Accuminata. (مفرده Condyloma Accuminatum)
  - ② Low grade IN

  NB:
  - Condyloma = knuckle.
  - Acuminatum = pointed.

- **High Risk or onCogenic types**
  - ≃15 types of HPV.
  - Commonest [16 & 18] (also 31, 33)
  - ① Bowenoid Papulosis
  - ② Bowen's dis.
  - ③ Buschke-Lowenstein Tm (استثناء سببه HPV 6)
  - ④ Intraepithelial Neoplasia → High grade
    - Vulvar IN (VIN)
    - Cervical IN (CIN)
  - ⑤ Digital Cancer

Condylomata Accuminata (Ano-genital Warts)

- Most Common STD among sexually active young adults in USA & Europe.
- Most infections are Latent or subclinical & this is Responsible for high incidence of Recurrence following Rx.
- (انا ♀) Genital HPV inf. of great importance in women than men d.t Risk of Cancer Cervix.
- Genital HPV inf. closely linked to Cancer:
  - Cervix
  - glans
  - anus
  - Vulvovaginal area.
  - Periungual area. *
- Natural Hx of Genital warts:
  - Most Cases → lasting 1-2 y. then resolve.
  - Few Cases → persist.
  - fewer " → Cancer.

(9)

© other factors that ↑↑ Risk of Malignancy of HPV:

1. Location of infection → . كانسر مثلاً (Highest Risk) < Transition Zone of Cervix; Anus
2. Smoking
3. Uncircumcision (in ♂).
4. Immuno suppression
5. Sex < early: before 17 y age; Multiple: أكثر من 6; ē Prostitutes.

· **HPV Types:** 30 types may be responsible for Genital warts & more than one type usually exist in one patient.

· **Type:** · HPV: 6 & 11 (Bg or Low risk to be transformed to Mg).

· **Site:** · may affect:

♂ → · penis · scrotum · anus · intraurethral (hematuria or Altered stream)

♀ → · vulva · cervix · anus · perineum · intraurethral.

· **C/P:** ③ clinical varieties: according to the site:

C/P → · Acuminate Type · Flat Type · Common Wart like

- ⓐ **on dry surfaces** · Penis · Scrotum
  ↓
  · Hyperkeratotic common-wart like papules
  · usually transmitted by contact ē common wart
  · HPV 2, 4.
- ⓑ **Flat ± pigmented** T/t. (SK like) → HPV 16 ✓

- ⓒ **on Moist opposed surfaces** (Perianal & Perineum) (60%) = "Acuminate Type"
  ↓
  Cauliflower mass
  · pedunculated
  · Flesh colored
  · Verrucous
  · Bleeds easily
  Signs of Mg: ① large protuberant masses ② Induration ③ Pain ④ Serosanguinous dis.
  → "Buschke Tm"

- **NB** Acuminate Type & Flat ±:
  · discomfort
  · discharge
  · Bleeding.

peroxidase

Bowenoid Papulosis (For details see Skin Cancer)

- HPV: 16 & 18
- Site: may be < Genital: Penis, Vulva & perianal
  Extragenital: Face & neck
- Clinically: Flat, (sessile), Hyperpigmented papules that difficult to be differentiated from Condyloma Acum.
- Path: Abnormal epithelial maturation & cellular atypia closely resembling Bowen's dis.
- Progression to Invasive SCC more on lesions of < Penis, Cervix, Vagina, Rectum.
- Females < with Bowenoid.
  with their husbands have Bowenoid → Risk of Cervical Dysplasia

Giant Condyloma Acuminatum of Buschke & Lowenstein:

- there is a type of SCC called "Verrucous Carcinoma" it can occur in 4 sites: (all may be caused by HPV):
  (Ackerman Tm) → ① oral cavity → Oral Florid papillomatosis
  ② Genitalia → Buschke & Lowenstein Giant Cond.
  ③ Planter aspect of foot (Sole) → Epithelioma Cuniculatum.
  ④ Gottron Tm: skin
- Verrucous Carcinoma ch. by < well differentiated
  slowly growing
  Locally Mg (rarely metastasize).

Giant Condyloma Acc. of Buschke & Lowenstein:

- rare aggressive wart like growth (Fungating condyloma like)
- Caused by HPV 6&11 (16, 18 with Carcinomas)
- Site < Common: Glans & prepuce (of) an Circumcised ♂
  Less ♀: perianal & Vulvar.

Peroxidase

سفرى

Genital warts in children

Transmission may occur:

1. Vertical transmission perinatally. (أثناء الولادة الطبيعية)
2. digital Autoinoculation
3. Fomites
4. Social non sexual contact.
5. Sexual Abuse. (مهم جدا)

· Transmission acc. to age:

· 1st year غالبا → Vertically
· Age > 3 Ys: غالبا → sexual Abuse.

- Spont. Resolution often in (75%) of cases.

NB annual Pap smear should be Taken From:

1. female ē genital wart or if Here Husband.
2. Homosexual Male ē Peri-anal Wart
3. Any genital wart in Immuno-suppressed

D.D of Genital warts = Causes of Papular / nodular Genital lesions

DD of condyloma acuminata

Sexually transmitted diseases

- Condyloma latum (syphilis): broad-based, smooth-surfaced lesion.
- Herpes simplex virus (HSV): vesicular eruption with red base and ulceration.
- Molluscum contagiosum: umbilicated yellowish papules with central core.

Common benign skin lesions

- Nevi: typically raised, but pedunculated types may occur.
- Ectopic sebaceous glands (Fordyce spots): small, yellow papules on genital and oral mucosa.
- Pearly penile papules: circumscribed papules, 1-2 mm in diameter, usually over the proximal edge of the glans penis (considered normal anatomy).

Neoplasms *(biopsy required if suspected)*

- Bowenoid papulosis: ~~carcinoma in situ~~, single or multiple rough papules, 2-4 mm in diameter, flesh-colored to red-brown, recalcitrant to usual wart therapies. (Flat, Sessile, Pigmented, Rough)
- Malignant melanoma: typically single, may be flat or raised with variable color and shape.
- Giant condyloma of Buschke-Löwenstein tumor: low grade, locally invasive malignancy that can appear as a fungating condyloma.

"do Biopsy if there is Controversy."

Cond. Accuminata	Cond. Lata
HPV	T. pallidum
Cauliflower	Flat
Flesh colored	Grayish
Verrucous Surf.	Smooth Surf.
pedunculated (c̄ its)	Sessile
bleed easily	don't Bleed esily.

- NB: Malignant transformation in nongenital wart is Rare But may occur & so Called: verrucous carcinoma that may occur on any area but commonest is plantar surface (Epethiloma Coniculatum).

- A typical, non Resolving wart on < hand / Periungual unit / Foot should be Biopsied to Roul out SCC c̄ can mimic wart specially in the Region of Nail unit.

peroxidase

Diagnosis of Genital warts:

① Acetowhitening:

Aim
- a. For detection of subclinical inf. of Genitalia.
- b. detection of early lesions under foreskin.
- c. determine extent of infect. in patients ē multiple Recurrences.
- d. define the area necessary for applicat° of Ttt

Method
- Acetic acid 5% (خل) applied for 5-10 mins → small macular white lesions.

False +ve
- May occur ē: Dermatitis, Candida, Psoriasis. if present: Antifungal + Hydrocortisone 1% → Repeat testing after 2 ws (if +ve) → Biopsy & Histopath. Exam. for HPV.

② Histopathology: (done before Ttt of any suspicious Lesions).

3 osis
- Acanthosis (+++)
- Papillomatosis (+++)
- Koilocytosis: Cells of st. Malpighii appear ē ch/c
  - Cytoplasm: Vacuolated, light-blue cytop.
  - Nucleus: Round & Hyper-chromatic ē Perinuclear halo.
- Others (See Cut warts).

③ PCR (detect viral DNA) [latent inf.]

④ Pap Smear for women (Even after Ttt). "مهم"

⑤ Sexual Partner Exam. for detect° of any subclinical inf.

NB: diagnosis of:
- Subclinical inf. BY acetowhitening
- Latent inf. BY
  - PCR
  - Immuno-peroxidase

  → detect the viral DNA inside the Nucleus.

Treatment of Cutaneous warts

* **Medical Ht**
  - Benign neglection
  - Topical
  - Intralesional
  - systemic
  - Alternative.

* **Surgical Ht**
  - Cryosurgery
  - Electrosurgery
  - Excision surgery
  - Lasers.

المطلوب كلمة بسيطة عن ميكانيزم
وكيفية الاستخدام.

Principals of Ht (إفهم كويس)

① Warts ar Benign cut. growths; so the Ht should be:

Benign: ??
- no scarring
- no hazards to patient.

[Side effects should be minimal.]

② inform the patient about (high) incid. & Recurrence (d.t latent infection in perlesional & NLLY appearing skin).

③ No specific Antiviral Ht for HPV; the Existing modalities focus primarily on
- → Removal or destruction
- → Immunomodulation.

④ No evidence that: Extensive Ht Results in better outcome.

مهمة للمرضى ⑤ with any modality: لازم العلاج يستمر لفترة (٢-٣ شهور).

Medical Ht

I Benign neglection:

- no Ht For warts may be carried out as this < Safe / Cost effective

why ?? because Most warts (65%) Resolve ein 2 Years.

but this Method may carry a risk of Transmission & autoinoculation

. So indications of Ttt are:

- Pain
- interference with function
- Social Embarrassement
- Risk of autoinoculat.
- Risk of malignancy

2. Topical Ttt

غالي / عالعيادة

. Physcian's applied (5) < C, 2T, 2P

a). Canthridine 0.7% (Cantharone):

extract of blister beetles (spanish Fly) → epid. Necrosis → Blister formation.

◎ ميكانيزم بطريقة تشبه الـ Cryo مرة

applied to wart → leave to dry & Cover For 24 hrs → (24-72 hr) blister → Repeat (Ttt) after 2-3 ws.

b). Topical Immunotherapy (High Conc. 2-5%) < DNCB, SADBE, DPCP

[تركيز عالى / رشة كل يوم / نقطة / ع رأس]

++ immune system by induction of Contact sensitization.

c). TCA: Caustic → tissue (50-80%) necrosis.

d). Podophyllin: Cytotoxic (used more ē Genital wart)

e) ALA (PDT): photosensitizer + Blue light (400-700 nm)

→ يوضع على السطح طبقة ٤ ساعات ثم يعرض للضوء .. مرة كل ٣ أسابيع

. Patients applied (5) → غالي / عالبيت

a) Keratolytics.

b) Imiquimod 5% Cream (Aldara) — مرة

. Immune Response modifier

. Used For < Genital wart (documented), Common wart (Some reports)

[رخيص ومتاح في صيدليات مصر / استخدام]

c) Cidofovir: For Recurrent & persistent. (under trials)

d) 5-FU: Cytotoxic chemotherapeutic

For < Flat warts (++), Common warts (+), Intraurethral (++) حقنة

S.E. irritat. & ulcerat.

e) Tretinoin: . كلنا بنرفع / لأعلى تركيز الا لما يحدث إحمرار خفيف

NB

. TCA: ممكن يستخدم عالبيت ايضا

. Topical Immunotherapy: ممكن بالبيت بتركيز اقل

* Keratolytics in warts:

(a) . Mechanism < Mechanical: Removal of infected cells & wart virus / induction of inflamm: → ++ immunity

(b) . Commonly used: Salicylic acid (S.A):

زى بكوريند مكلوكلوديان → . Paint: S.A 16.7% + Lactic acid 16.7%
. Plaster: 40% S.A.

تركيبة:
- . S.A: 20%.
- . Lactic: 5%
- . Base: Flexible Collodion.

(c) .. Method:

(١) تنقع القدم في ماء دافئ لمدة ٥ دقائق أو أكثر مساءً
(٢) يتم حك السطح بالحجر [حجر الكعب أو المبرد]
(٣) توضع الدهان باستخدام عود كبريت بعد إحاطة الجلد السليم بفازلين ويترك ليجف
(٤) يفضل وضع بلاستر (occlusion)
(٥) تكرر العملية كل مساء مع إزالة أي تقشور بالحجر أو المبرد قبل الدهان الجديد [لإزالة الطبقة المتقرنة]
(٦) عند استخدام البلاستر: (40% S.A): توضع لفترة تمتد لأسبوع [وتكرر] — مهمة جداً
(٧) عند حدوث احمرار بالجلد نوقف العلاج إلى أن يختفي الالتهاب — دائماً أستخدم

. under occlusion . S.A 40% + TCA 50% → لفترة حوالي ٢-٣ شهور → نتيجة حوالي ٧٠-٨٠٪

↑ Multiple agents under occlusion

(NB) : . Immunotherapy
- DNCB: dinitrochloro Benzen.
- DPCP: Diphen Cyprone.
- SADBE: Squaric acid dibutyl ester.

. TCA: Trichloracetate (50-80%) : (تباع التقشير - عند الطرشوب)

. ALA: Aminolevulinic acid.

. Imiquimod (يشفى أو تحريري) 5% (Aldora®)
- Aldora® 5% Sachet
- Zyclara® 3.75% C.

. Immune Response modifier → act on Toll like R's of Immune Cells.
. exact mechanism unknown
. thought to → Cytokines Release: by KCs & Virally infected cells:
- . IL 1, 6 & 8, 12
- . IFN-α
- . TNF-α
- . GMCSF

→ Viral elimination.

Intralesional ⊠ (Extensive, Resistant)

(1) Antigens: Candida, Mumps – (MMR Vaccine), Trichophyton, PPD (Tuberculin) → مستشفى الصدر "الجامعي", BCG

(2) Bleomycin:

- Cytotoxic (↓ DNA synth.)
- For: recalcitrant common warts (مكلفة)
- Concentration: 1 U/ml (1 mg/ml)
- For small warts (<5 mm) → inject 0.1 ml
- " Large warts → " 0.2 ml
- don't exceed 1-2 ml / session, or 0.2 ml - 1 ml / lesion.

جلسة كل ٢-٣ أسابيع غالباً بيحتاج جلستين فقط

(128) (85) ج Bleocin & Bleocip

الأفضل يحضروه معاهم. ليكون بارد ويكون ما يقلل الألم (Anaesth → disrupt CM → ↑ efficacy) على دكتور شهرية.

Minimum 1 ml / lesion: → 0.2 ml – 1 ml.

طريقتين:

- Intradermal: Into & beneath the lesion
- Multiple puncture Technique: نضع نقطة على السطح ثم يتم وخز السطح بالإبرة

→ till blanching → (علامة النجاح) Black crust separates into 2-4 ws [جلسة كل ٣ أسابيع]

S.E:
1. pain (use local anaesth.) (تعمل سيطرة مرادفة)
2. digital warts → Raynaud's phenomenon or Gangrene.
3. Cellulitis & Lymphangitis
4. Patients received >14 ml → Flagellate urticaria → chic Flagellate Hyperpigm, urticaria, Anaphylaxis.

Other uses (Tms):
- BCC, SCC, AK, Bowen's, K.S, Hemangioma.

(3) IFN-α2b: Naturally occurring cytokines that has

Actions:
1. antibacterial
2. antiviral
3. anti cancer
4. Immunomodulatory

مليون وحدة ٣ مرات كل أسبوع

(4) IPL & laser ##.
↓ PDL

pulsed dye.

(نادراً)

Systemic Tt (Immunostimulant)

1. Cimitidine : in large doses (600mg/d) → Immunomodulatory effect. (30-40mg/Kg/d)
2. Retinoids : For extensive, Hyperkeratotic disabling Lesions in immunocompromised ←
3. IV Cidofovir (under trial).
4. Zinc Sulphate : (Some Reports) : 10mg/Kg/d (maximum 600/d) "for plantar warts". — Topical (10%), oral (10mg)
5. Levimasole (Ketrex) : 5mg/Kg in 3 consecutive days / 2ws for (5ms)

Alternative therapy

Mechanism:
1. autosugg.
2. Suffocate
3. debridement

1. Adhesiotherapy : duct tape (not permeable & water proof)
   - Good Tt specially < Children / inability to use Tt.
   - يوضع لمدة اسبوع
   - الاكياد
2. Hypnotherapy (Autosuggestion) : For Refractory warts.
3. Thermotherapy : (بالحرارة...)
   - إحدى طريقتين <
     - Localized Heat therapy : * موضعية لفترة ٣٠-٦٠ دقيقة ٣ مرات يومياً
     - Water Immersion : يتم غمر القدم في ماء ساخن [٤٥°] لفترة حوالى ٣٠ دقيقة [٣ مرات اسبوعياً]
4. Garlic : Raw garlic gloves put on wart under occlusion.
5. Vaccines : (under trials).

Surgical Tt

* Cryosurgery
- Best & 1st line of Tt
- not only destroy the virus but the cells containing it.
- Freeze time : 10-30 sec. (Face ← / → plant)
- No of cycles : 1 /session. (2 plantar)
- No of sessions : 3 (واحدة كل شهر) (1-4w)
- Rim : 1-2mm around the lesion.

* Electrosurgery
(Electrodissication & curettage).
- Effective but :
- S.E < pain, scar, viral isolat. from plume.

* Lasers
"غالي"
- indication : Large or Refractory lesions
- disadv : expensive & plume it.
- Type : CO2 laser, Nd:Yag, Pulsed dye.

* Excision surgery
→ Avoid it → Scarring, Recurrence.

Treatment of Condylomata.

- Goal of ttt: Removal of exophytic lesions & Amelioration of symptoms.
- no ttt has been shown to eradicate HPV Completely d.t Common Latent & subclinical infection. (So) it may be Considered. (Friend of Life) (as H.SV2)

قراءة

- Prevention: * Value of Condom
  - not prevent inf.
  - ↑↑ Regression of Flat penile lesions & CIN.
  - Clearance of Couples infected c̄ the same HPV.

  * Limiting No of Partners: remains mainstay to ↓↓ Transmission.

ttt

الجسم يتخلص من الـ ttt في 5 شهور

Patient applied Agent

(1.) Podophyllotoxin (Podofilox, Condylox)

0.5% sol. or gel.

دهانه مرتين يوميا لمدة ٣ أيام متتالية
ثم راحة ٤ أيام ويتكرر الدورة لمدة
٤-(٦) دورات

- C.I
  - pregnancy
  - area > 10 Cm²

(2.) Imiquimod

Mucosal Genital wart

أفضل من Cut. wart

- 250 mg Sachets: → ⊙ دهان مرة يوم بعد يوم لمدة (١٦) أسبوع
  - (12.5 mg الواحد)
  - Contain 5% Cream
- Rectal suppositories: ↓↓ Recurrence of Rectal Condyloma in immuno-Compromised.

Physician applied.

(1) Cryo: ttt of Choice for pregnant

(2) podophyllin 25% in Tr. Benzoin or Collodion or Alcohol

(3) TCA (80-90%):

- مرة كل أسبوع (من ٦ مرات)

Used for:
- Pregnant
- children.

(4) Surgery: endoscopic Removal

(5) Electro

(6) CO2 Laser

(23)

1 million IU 3times/w For 3ws. → (7) Intralesional interferon (Intron α2b)®

(8) 5FU.

(9) ALA (Photodynamic)

NB. on the ttt

what the difference between "مهم"

Podophylline Resin (25%) in Tr. Benzoin (مادة الخام)

- Crude extract of dried roots of the May apple plant.
- Contain many ingredients: the most active is Podophyllotoxin
- Used ē
  - Tr. Benz
  - Alcohol (10-35%)
  - Collodion
- دهن مرة كل اسبوع تشطف بعد حوالي ④ ساعات وتكرر لحد اقصى ⑥ مرات
- C-I
  - Pregnant (Teratogenic & death) (X)
  - area > 10cm2
  - ulceration & Bleeding
- Less effective in dry surfaces: glans, scrotum & labia

Podophyllotoxin 0.5% (مادة اطنقاه)

- purified extract of Podophyllin resin (the most active ingredient in it)
- So don't contain any of the ingredients responsible for toxicity of podophyllin
- More effective > Podophyllin
- عشان كده نفضل عدم استخدام: Podophyllin Resin

Imiquimod → See Mechanism → احمل كارية

Common wart

دهان مرتين يوميا لمدة 5 اسابيع

(Cryo / SA كريم)

Genital wart

- دهان 3 يوم بعد يوم لمدة ⑯ أسبوع
- لبوس شرجي (↓ Recurrence)

• Imiquimod S.E:

- mild - mod. irritation
- Rare:
  - Flaring of Ps.
  - Hypo pigm. (like vitiligo).
  - Neuropathy
- Other indicat. : AK (if very scaly Cryo 3 wks → Imiq.)
  - AK: [illegible]
  - Bowen's & BCC [illegible]
- EFFICACY : بالترتيب

Podophyllin < Imiquimod < Cryo < Electrocauterization

Poor Penetration of non-mucosal Skin So:
- Use it + S.A or
- Cryo + Aldara & occlude.

• 5 FU

1. Flat, Hyperpigmented lesion of Bowenoid.
2. Intra Urethral wart

↓

[illegible]

Continuous therapy
twice daily instillation of 5FU in the urethra
↓
irritation.

Intermittent therapy
twice weekly instillatⁿ of 5FU in the urethra
↓
NO irritation

- يمنع التبول بعد العلاج لساعة
- تجنب تلامس البول مع كيس الخصية

IMIQUIMOD

- INTRODUCTION

Imiquimod (1-(2 methylpropyl)-1 H-imidazo [4, 5c] quinolin-4 amine) is an immune response modifier that stimulates innate and adaptive immune pathways, resulting in antiviral, antitumor and immunoregulatory properties.

- **Mechanism** → Act on Toll-like Receptors 7 & (±8) (TLRs 7) [expressed on surf. of < Lymphocytes, Macrophages, dendritic cells]

↓ ++ Innate Immune System
1. ↑ IFN-α, TNF-α, IL6, 1, 8, 12
2. ++ NK Cells
3. ++ IL10 sec. by Macrophage.

↓ ++ Adaptive Immune System:
- Imiq + Immature APC → Mature APC → ++ Naive TC → Th1 Activat^n^
- ↓ IFN-γ

↓
1. Antiviral. [viral wart AH]
2. Anti Tm [< AK, BCC]. Viral
3. Immunoreg.
4. Antiproliferative

x) **Other mechanisms:**

1. in Keloid: ↓ VEGF, ↓ GAG, ↓ Coll.
   - Imiq. → IFN → anti angiogenic effect (↓ VEGF which is ↑ in epid of Keloid).
   - Imiq. → ↓ Coll synth. & GAG synth.
2. Induct^n^ of Tm suppressor funct^n^ via Notch-signaling pathway
3. Recently: Antiproliferative & antiviral d.t (↑↑) OGFr

• preparations.

1. Aldara®: Imiq. 5% Cream.
2. Zyclara®: " 2.5% & 3.75%

تركيزه أقل يعتمد
استعماله على مساحة
أكبر لعدد مرات أكبر
لكنه أقل فاعلية
↓
(Aldara < 25 cm²)

• Indications & Methods:

- FDA approved ← 2 AK, 3 Wart, 5 BCC
  1. Ano-Genital Warts
     - Imquim. 5%
     - دهان ٣ مرات في الأسبوع لمدة ٤ شهور
  2. AK
     - Aldara ↓ دهان مرتين في الأسبوع لمدة ١٦ أسبوع
     - Zyclara ↓ دهان يوميا لمدة أسبوعين ثم راحة أسبوعين وتكرار.
  3. BCC [non facial < 2cm] ↑ شرط
     - Aldara ↓ دهان عليها وحواليها ١ سم ٥ مرات كل أسبوع لمدة شهر ونصف
  4. Bowen
- Non FDA (offlabel uses)

في كل الأحوال ← يترك الدهان لمدة ٨ ساعات (٦-١٠) [فترة النوم] ثم يشطف. [يعمل حساسية للشمس]

• Non-FDA approved:

- Keloid → بعد الجراحة يوميا لمدة شهرين
- Common warts
- Porokeratosis.
- Molluscum
- SCC (insitu) → "Bowen's" (مرة يوميا لمدة ٤ شهور)
- EMPD.
- Xeroderma pigm.

Adverse Effects

Topical: >10% (all at application site) Erythema (54-61%) Erosion (29-31%) Excoriation/flaking (18-25%) Edema (12-17%) Itching, burning	Systemic absorption (minimal) Headache Flu-like symptoms (fever, fatigue) Myalgia Diarrhoea

Contraindications

- Not recommended for urethral, intravaginal, cervical, rectal, or intra-anal human papilloma viral disease
- Pregnancy & Lactation :Pregnancy Category: C, Lactation: not known if distributed in breast milk; use with caution
- External Genital Warts in children: <12 years: safety and efficacy not established

Cautions

- ✓ Avoid or minimize exposure to sunlight, including sunlamps
- ✓ Do not use until skin has fully healed from any previous drug or surgical treatment
- ✓ Safety/efficacy not established for other forms of BCC besides sBCC
- ✓ Safety/efficacy not established for sBCC lesions on head, face or anogenital area
- ✓ Dosage is different for different indications
- ✓ Avoid sexual contact while cream is on skin
- ✓ Severe local inflammatory reactions of the female external genitalia can lead to severe vulvar swelling; severe vulvar swelling can lead to urinary retention; dosing should be interrupted or discontinued for severe vulvar swelling

Immunotherapy For Cut. Warts

Topical < Sensitizers / IRM

(1) Sensitizers:
- DCP
- DNCB
- SADBE

(2) Antigens: BCG & Tuberculin

(3) I. Response Modifier
Imiquimod.

Intralesional < Cytokines / Ag

(1.) Cytokines:
- IFNs α2b
- IL2

(2) Antigens:
- (i) Bact. : BCG
- (ii) Viral : MMR
- (iii) Fungal : Candida & Dermatophyte Ag
- (iv) proteins : Tuberculin & PPD.

Systemic

30-40 mg/kg/d = ÷ ... id
- Cimetidine
- → Levamisole
- Zinc Sulfate

. Mechanism : ?? ± d.f ++ Th1 & -- Th2 → Th1 Cytokines profile (IL2, TNFα- IFN-γ)

MMR

. Indicat: Recalcitrant & Extensive warts.

. Dose : 0.3ml - 0.5ml / 2ws till either < Clearance or 5 injects

. Methodology: Intradermal (or even S.C) at either The warts or NL Skin -

. SE (i) local : Pain, Erythema, Induration, ulceration, Dyspigm. & Scarring

(ii) Systemic
- Flue like S&S
- Anaphylaxis
- Autism (in Vaccines)
- Granulomatous Hepatitis

NB: . BCG: ++ more intense local React → Suitable for single or few warts

. MMR.: effective in eradicat of Both < local / distant warts.

Pox viruses

1. Molluscipox → MC
2. Parapox — orf virus, Milker Nodule virus.
3. Orthopox — Variola virus → Small pox; Vaccinia virus → Vaccine of Small pox.

Molluscum Contagiosum (MC)

- Viral skin inf. Caused by poxvirus (Molluscipox), family poxviridae.
- Etiopathogenesis:

- Virus: Cant be cultured on artificial media but on human foreskin. There are 5 types: type 1 (95%) of infections, type 2 (3%, the most common in HIV patients), types, 3, 4, and 5. No relationship between virus type and lesional morphology or anatomical distribution is known.
- Mode of transmission: contact (direct, indirect, autoinoculation), sexual transmission.
- Risky patients: children, immunocompetent adults and immunocompromised (HIV, leukemia, malignancy, sarcoidosis, atopics).

MC
- Id
- Inflamm.

C/P

- Asymptomatic, Dome-shapped, umbilicated, pearly white, small sized papules, that's if squeezed it extrude cheesy material. Both Skin and MM can be affected.
- Clinical varieties: giant MC (Lesion ≥ 1.5 cm), disseminated (in HIV usually facial and perioral, at eczema sites of AD), eczematous MC (type of infectious eczematoid dermatitis), inflammatory MC (inflammation, suppuration, and crustation, usually not due to 2ry infection rather than traumatic).

DD

- Viral warts, KA, coccidioidomycosis, cryptococcosis, histoplasmosis, perforating dermatoses

Investigations

1. Dermoscopy
2. Squash prep.
3. HP.

① Squash preparation:

microscopic examination of cellular exudate. The cellular material contained within the central umbilication may be extracted manually, flattened between 2 microscope slides, and stained. Microscopic examination of this preparation reveals the Henderson-Paterson bodies (intracytoplasmic inclusion bodies).

② Dermoscopy: Central yellow-white lobular structure surr. by crown of Vs

② HP: cup-shapped indentation of the epidermis into the dermis forming a crater. Within the region of the indentation, the epidermis appears thickened (acanthosis), and the cornified layer typically is disintegrated. The striking feature is the presence of intracytoplasmic, eosinophilic, granular inclusions within the keratinocytes of the basal, spinous, and granular layers of the epidermis.

These inclusions, **the Henderson-Paterson bodies**, can measure 35μm in diameter. Ultrastructural studies have shown that these bodies are membrane-bound sacs that contain numerous MC virions. The viral particles increase in size as they progress up toward the granular layer, causing compression of the nucleus to the periphery of the infected keratinocytes. The surrounding dermis is relatively unremarkable. Intact lesions show little or no inflammatory change.

HP
- as warts
- also
KOH 10%.

Orf (وهمانه بتاع جرابي)

- **Et.** Orf virus (Parapox virus)
- **Source, Mode & risk pts:**
  - Contact ē infected animals < Sheep (خرفان) / Goats, Carcasses (Sheep head ↙ الذبيحة), Pasture (مرعى / وهوصا)
  - **pts:**
    - Young-Lambs اللي تيجي الفلاحين ترضع
    - أطباء البيطريين و الجزارين (وخصوصا ختم الراس)
  - **No** Transmission to Cattle or [human-to human] ZZ
- **C/P:**
  - **IP:** 5-6 ds.
  - **Site:** hands, Arms & ± face.
  - **Skin lesion** ± L.N / Lymphangitis ± Fever (أكثر)
    - ↓
    - firm, solitary or few, red-blue papule(s) of (dorsal hand)
      → H̄gic, Flat-topped pustule or bullae that ± show Central Crustat^n.
  - lesion ±: < Tender & Bleeds easily.

Firm Nodule (red-Blue) ↓ ± H̄gic < Bulla or Pustule & crustat^n:

غالبا صعب نمت الكلام وتلاقي تكتبها "Firm Nodule"

Stages ≃ 6 each one lasting ≃ 1/wk

- stage 1: Maculopapular.
- stage 2: Targetoid lesion.
- stage 3: Acute weeping nodule
- stage 4: "regenerative stage"; Nodule ē crustat^n & Black dots.
- stage 5: Papillomatous
- stage 6: "regressive": thick crust covers the regressed lesion.

Complications —
- BP
- EM
- Disseminated Cut.
- Toxic erythema after 10-14 ds.

Inv:
- **HP**: pseudoepith. Hyperplasia, ulcerat^n, Necrosis, vacuolizat^n & disintegrat^n of KCs., Intracytoplasmic & Intranuc. IC.
- PCR & DNA Hybridizat^n (differentiat^n bet. it & Milker's Nods).

Treatment:
- Reassurance (self, limiting)
- dressing & Antiseptic
- Excision, Cryo, Curett for exophytic lesions

Milker's Nodules
- as orf but differ in:
  - (1). Virus .. ??
  - (2). Transmission by: "tits of cow".
  - (3). PCR & DNA Hybr. بنفرق بينهم

Viral Exanthema

- Viral Inf. ± associated with
  - Cut. Eruptions (rash) → Exanthema
  - Mucosal Erupt. → Enanthema.
- Most Viruses produce similar rashes; so the Term "Non specific Viral Rash"

Types of Viral Exanthema

(1) Vesicles on Erythematous base → HSV, VZV, HFMD

شبكية

(2) Lacy Erythema → Erythema Infectiosum

"Scarlatiniform" → (3) Diffuse Erythema → HBV, Entero & Adeno Virus.

(4) Acrally located papules → Gianotti Crosti (PAC)

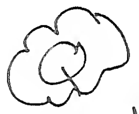
(5) Morbilliform (Maculopapular) →
- Measles & G. Measles.
- Erythema Infect.
- Roseola Infantum.
- PR.

DD of Morbilliform Rash

(1) Viral [illegible]

(2) Drug: NSAIDs, Ampicillin, Amoxicill., INH, Thiazides.

(3) others: (rare)
- Kawaski
- GVHD
- DRESS



طفل سخن
وخد مضاد حيوى
وبعدين طلعله
Rash ??
من الفيرس ولا الدوا ؟

→ **DD: of Drug & Viral Induced Morbilliform Rash. ??**

(1). Childhood Age
(2). Fever
(3). No itching
(4). Mucosal affect.

→ all with Viral Exanthema > Exanthematous Drug Erupt.

Viral Morbilliform Rash

بلاش تفاصيل واعرف أهم الخصائص لكل نوع ؟؟

- Measles (Rubeola) (1st dis.)
- German Measles (Rubella)
- Erythema Infectiosum (5th dis)
- Roseola Infantum (6th dis = Exanthema Subitum)

أهم خصائص كل نوع

A. Erythema Infectiosum

- Parvovirus 19
- Slapped cheeks
- Lacy (reticulated) Erythema
- No MM affectⁿ.

B. Roseola Infantum (Exanthema Subitum)

- HHV 6 & 7.
- Age <3 (usually < 6m .. سن صغير جداً)
- Rash begins with drop of fever.
- MM → Nagayama's Spots (red papules on Soft Palate).

- **NB** Parvovirus 19 also Causes "Papular purpuric Gloves & Socks Synd."

Milder but Serious on pregnancy. 5

	Measles (Rubeola)	German Measles (Rubella)
. Virus	. Paramyxovirus (RNA)	Toga virus. (RNA)
. IP	. 2-3 ws.	1-2 ws
. Infectivity period.	. 5 ds before to 5 ds after rash	. 2 ds before & 4 ds after
. Prodroma	. Fever, Cough, Coryza, Conjunctivitis (3C) (Serious)	. Children: mild - Absent . Adult: FAHM, Nusea, Pain at lat. neck ... Painful occipital L.N
. Enanthema	. Koplik's spots: grayish-white papules at buccal mucosa at eryth. background "2 ds" before & 2ds after rash.	. Forsheimer spots: petichae on Hard palate or Soft palate (Petichae → palate)
. Exanthema	. Maculopapular rash, starts postauricular & at Ant. Hair lines 3ds → Spread to all over the body 5ds → يبدأ يختفي بترتيب	. Maculopapular rash starts & spread caudally from face to all over the body 1-3d → يختفي بترتيب . Rash is absent in 40%.
. Complications	. OM, pneumonia . Encephalitis. . Panencephalitis (بعد مدة)	. Arthritis, Encephalitis, Thrombocytopenia & Cong. Rubell Inf. (if 1st Trimester) [Cataract, deafness, CHD, Anemia, Thrombocytopenia & Muffin. baby synd.) "blue Berry"
ttt	(i). vaccinate (MMR: 12-15 ms) (ii). Supportive & Vit A	(i). Vaccine (ii) Supportive

NB1) Unilat Laterothoracic Exanth. (Asymm. periflexural Exanth. of Childhood)

- Etiology ??
- prodroma (URT & GIT) → unilat. morbilliform or Eczematous rash that starts unilat (Axillae > Trunk > thigh) → spread to / Contralat. Sites 3-8 w → spont. Resolution

NB2:) • Enteroviruses (RNA, Coxsackievirus, Echo, Feco-oral & droplet):

- HFMD & FMD
- Herpangina
- Eczema Coxsackium
- Int. organs: RT, CNS, GIT.

Hand-foot & Mouth dis (2014) (HFMD)

- oral vesicular disorders caused by picornavirus (Echo-Entero V.) (RNA)
  - (i). HFMD
  - (ii). Herpangina
  - (iii). FMD

Causative virus (Enteroviruses)

- (i). Coxsackievirus A16 → most common (Entero)
- (ii). Cox. A6 → severe affect, extend (face, perioral, limbs) (vesiculobullous) (eczema coxsackium)
- (iii). Enterovirus (EV-71) → sepsis (neuro-complicat.)

Mode of Transmission

- (i) Fecal-oral route
- (ii) Contact ē infected skin lesions or oral secretions.
- (3) droplet.

C/P: . Age < 10 y. (95% < 5y.)

. prodroma: FAHM, sore throat & ± diarrhea.

. Rash: Tender/painful macules & vesicles at buccal mucosa, palate, pharynx → Hands & Feet (palms & dorsal aspects) → Erosion & ulcerat. 1w resolution.

- on erythematous base.
- Other areas (leg, buttock, genitalia)

Other features:

1. onychomadesis
2. Neurological complicat. (ē EV-71)

D/D (Ø is mainly clinical):

- (i) leukocytosis, lymphocytosis, ↑CRP & ESR
- (ii) Viral isolat.: Culture, Immunoassay & PCR (detect EV-71)

TTT → supportive measures

- Antipyretic
- Analgesic
- IV fluid
- Amantadine & Ribavirin ??

NB

1. one Hand & 2 Feet Synd → Fungal inf.
2. Hand-foot Synd: pp. Erythema Induced by chemoTT (DNNZ)
3. Foot & Mouth dis: . serious, Epidemic, rare in human, contact ē infected "stock" 1w cows

Gianotti-Crosti syndrome

(PAC: Papular Acrodermatitis of childhood)

Causative virus: (1) HBV (ayw strain), EBV, Entero (Coxsackie A16), Echovirus, RSV

(HBV, EBV & vaccine)

(2) Bact. - Bartonella & Mycoplasma, strept. (3) Vaccinat.

Age: 2 - 6 years. (6m - 12y)

Clinically

1. Non-pruritic erythematous papules (or pap.vesic) on face, buttocks and limbs lasting about 3-8 weeks. Fading with desquamation.
   - Extensor
   - Buttocks
   - Face
   - Spare: Trunk, Elbow, Knee, PP
   - Severe affect. is against Ø.
2. Enlargement of inguinal or axillary lymph nodes. (L.N), HSM, fever, ± tachic
3. Acute hepatitis lasting for 2 months.

Diagnosis . HBS Ag

TTT → Conservative.

Cutaneous manifestations of hepatitis B &/or C infection (see also p. 19 in "Dermatology & Internal Medicine")
• Mixed essential cryoglobulinemia.
• Cutaneous small vessel vasculitis.
• Urticarial vasculitis.
• Porphyria cutanea tarda.
• Polyarteritis nodsa.
• Lichen planus.
• Serum sickness-like syndrome.
• Gianotti-Crosti syndrome.
• Pruritus.
• Erythema nodosum.
• Erythema multiforme.

Pityriasis rosea

(PR)

An acute, self-limiting, papulosquamous eruption with a duration of 6-8 weeks.

Pathophysiology...??

- Viral: PR has often been considered to be a viral exanthem, a view supported by the condition's seasonal occurrence, its clinical course, the possibility of epidemic occurrence, the presence of occasional prodromal symptoms, and the low rate of recurrence upper tract respiratory infections (old speaking was regarding HHV6,7, and Picronavirus...but no evidence auggested).
- Drugs : drug induced PR.

Clinical presentation: A single scaling patch (the herald patch) appears 1-10 days before the general rash. It is an oval pink or red plaque 2-5 cm in diameter, with a scale trailing just inside the edge of the lesion. The herald patch is often mistaken as ringworm. It can also be confused with psoriasis.

A few days later, more scaly patches (flat lesions) or plaques (thickened lesions) appear on the chest and back. A few may also appear on the thighs, upper arms and neck but they are uncommon on the face or scalp. These secondary lesions tend to be smaller than the herald patch. They are oval in shape with a dry surface. Like the herald patch, they may have an inner circlet of scaling. These lesions follow the relaxed skin tension lines (Langers lines) on both sides of the upper trunk so that the rash has been described as looking like a fir tree or "Christmas tree".

PR is usually asymptomatic but may be itchy . In white skin the patches are pink or red, but in darker skin they may be pigmented or they may appear white due to the scale. Postinflammatory hypo/hyperpigm. May occur.

- Recurrence : 2% but Relapse of fading Eupt± occur.

Clinical varieties:

- Abortive PR: herald patch only, no 2ry eruptions.
- Inverted PR: affect acral areas (face, palmoplantar...DD; $).
- Localised: cervicofacial or girdle (axillae and groin).
- Generalized .
- Segmental, unilateral and Blaschkoid
- Short course (1-2ds) & persistent PR (ms-ys, often drug induced).

- Multiple Herald patches or No Herald Patch (2010)
- Giant PR of vidal (pit.Circinata et marginata of vidal, limb-girdle PR): A morphologic variant characterized by atypical large patches that tend to be fewer in number and coalescent has been described. In this variant, commonly referred to as pityriasis circinata et marginata of Vidal or, the eruption generally appears in the axillae, the groin, or both, with the trunk and extremities usually spared.[32] Individual patches are 3-6 cm in diameter, exhibiting the characteristic central clearing and collarette of scale with surrounding erythema.

  - Few
  - large
  - persistent
  - Localized but ± generalized
  - DD. T.Circinata
- Variations in the lesions: papular, vesicular, pustular, bullous, purpuric, urticarial, EM like, lichenoid, photoexacerbated, oral, vulval and penile.

DD:

- *2ry syphilis:* no herald patch, palmoplantar predilection, generalized LN, other manifestations, serology.
- *Pityriasiform drug eruption* (ACEI, ketotifen, bisthmus, gold, barbiturates): no herald patch, marked itching, lichenoid rash, prolonged course, postinflamm. Pigm.
- *Pityriasiform SD:* no herald patch, at midline trunk, other seborrheic areas. (± Scalp, dull in Color, Thick "greasy" Scales)
- *Others:* guttate Ps.& T. corporis.

· NB: PR in 1st Trimester ± → Abort or premature

Treatment

1. Reassurance: → self limiting.
2. Symptomatic tt: Antihistamines & Topical Cs
3. Erythromycin: 250 mg X 4 /d X 2 w (Earlier initiat → ± Complete Clearance)
4. NB-UVB: ↓ Severity but ± → Hyperpigm.
5. Systemic Cs & Dapsone: For wide spread & Eczematous PR
6. "Acv": in 1st week, 1gm or 400 X 5 X 7

Vaccines in Dermatology

- HPV → عرض أول عامهم

TB

(1). BCG (Bacillus Calmette G.)

(2). live attenuated (LAV)

- الجرعة : أول يحقن بالجلد بعد الولادة أو بعد ذلك لو عنده خطر العدوى
- استعمالات أخرى : يحسن المناعة في حالات السنط وسرطان البروستاتا

Leprosy

(1). BCG

(2). BCG + Killed M. leprae (Convit)

(3). Tawalars (M. welchii strain)

(4). Subunit vaccine.

- يعطى لأي حد معرض للعدوى
- أو عايش في منطقة Endemic

HSV (under trial)

- Killed whole vaccine
- LAV
- Recombinant Glycosylated subunit.

أي حد معرض للعدوى .. لأن زوجته مثلا هي Sero -ve وجوزها +ve مثلا

Varicella

طبعا معروف ..

(1). VariVax] LAV

(2). MMR-V]

- يعطى عند سن ١٢ - ١٥ شهر
- ويكرر عند ٤ - ٦ سنوات
- Prevent infection or severe attacks
- ↓ incid. of PHN

HBV

- Subunit.
- Recombinant.

* 3 IM doses at: 0, 1, 6 m.

أي حد بيتعامل مع دم أو معرض للعدوى زي الغسيل الكلوي

HIV (under trial)

- AIDSVAX : gp120 subunit.
- Subunit
- Recombinant

- أي حد معرض للعدوى (طبعاً معروفين)
- ليه صعب تصنيعه بقى كلام نظري في كتاب STDs

MMR

- LAV
- Dose: as Varicella

Acne

. "Component" Vaccine:
- "Inactivated" whole Bact.

بيشتغل عازاي

↓ IL8 & MIP2 (Macrophage Inflammatory protein) Released By P. Acnes.

Melanoma

. Whole Cell Tm Vaccines
. Autologous Tm Vaccine
. Allogenic ~ ~
. peptide Vaccines
. Ganglioside ~

. Indicat: Metastatic Melanoma
يحقن عضل أو تحت الجلد أو بالحلد
في أي Limb بيعدي الخلايا MM

. HPV Vaccines

- 3 Types ← Cervarix (2), Gardasil (4), Gardasil (9)

Cervarix (2) (16,18)	Gardasil (4) (6,11,16,18)
. No protect against 16,18 Genital warts	. protect. (6,11,16,18)
. 0.5ml, IM: 0,1,6ms	. 0,2,6 m.
Age approval: ♀ 10-25 Y.	. ♀: 9-26 . ♂: 9-15
. Elderly: ♀ 26-55	. Not recommended for ♀ > 26

(NB) Gardasil is of 2 Types:
1. Gardasil 4 (6, 11, 16, 18)
2. Gardasil 9 (6, 11, 16, 18, 31, 33, 45, 52, 58)

(1). Type: (Purified product Major Capsid protein L1)

(2). ممنوع ممارسة الجنس الابعد استكمال الثلاثة جرعات يعطى نتيجة تمتد إلى ٨ سنوات

(3). Given in infect ??? ⇒ Residual effect ↑
↳ protect from other strains from which the pt. doesn't Infected.

S.E
(1). local react.
(2) Syncope
(3) Thrombo-embolism.

(٨)

اسئلة امتحان

(A) EBV (HHV4) diseases caused by it

1. IM = glandular fever

Triad: Fever, L.N, Pharyn.

- Rash → Morbilliform (if given penicillin ← بعد اسبوع) كل الحالات
- Tonsillitis
- Hepatitis
- HSM
- Petichae < Skin, MM
- lymphocytosis ē Atypical lymphocytes.

2. Others:

- Urticaria & UV
- EM & EN
- PAC & CBDC
- BCL & PLC
- Hairy leukoplakia
- Hydroa vacciniform
- Reactive genital ulcers.

Diagnosis

Anti- EBV Abs

(1). Paul Bunnel test (sheep RBCs)

(2) Monospot test (Horse RBCs).

> • Hogland sign: EBV ass. ē Bilat. Eye Edema

(B) CMV

- ✓ IM like < less severe, No Tonsillitis, " Hepatitis
- ✓ In Immunocompromised: Colitis, retinitis, pneumonitis.
- ✓ Cong & Neonatal: < IUGR, Jaundice, Thrombocytopenia.

(C) HHV6 & 7

- Roseola Infantum (HH6 > HHV7)
- DRESS
- PR.

امتحان

(D) HHV8 <
- K.S
- Lymphoma (1ry effusion)
- Multicentric Castellman dis. (Lymphoprolif. dis: Fever, L.N, HSM)

Pox virus (د)

Type

1. Parapox : Orf virus, Cowpox virus (Bovine papular dermatitis virus).
2. orthopox : Small pox virus (Variola), Vaccinia, Cowpox, Monkeypox
   - Vaccinia → Live virus used for Variola vaccine.
     - C/P: ① local react at site
     - ② Eczema-vaccinatum in AD.
   - Cowpox → Cats, Cattle, Rodents. → • Papules, • Pust., eschar (Black).
   - Monkeypox → Rodents.
3. MolluCipox : MC virus
4. YatapOX.

- General ch: : . Double stranded DNA
  . Small pox & MC are specific to Human.

في الجدبي اللي ريوناء

1. Orf virus (Ecthyma Contagiosum)
2. Milker's Nodule virus (cowpock)
3. Molluscipox (MCV)
4. Smallpox (Variola) مع القضاء عليه

Orf

- Et. Orf virus (Parapox virus)
- Source, Mode & risk pts.:
  - Contact ē infected animals < Sheep, Goats, Carcasses, Pasture
  - Pts: Young Lambs
    1. أطباء البيطريين والجزارين (وخصوصاً لحم الرأس)
  - No Transmission to Cattle or human-to-human
- C/P:
  - IP: 5-6 ds.
  - Site: hands, Arms & ± face.
  - Skin lesion, ± L.N / Lymphangitis ± Fever
    - firm, solitary or few, red-blue papule(s) at dorsal hand
      - → Hyic, Flat-topped pustule or bullae that ± show Central Crust"
    - lesion ±: < Tender & Bleed easily.

Firm Nodule (red-blue) → ± Hyic < Bulla or pustule ± Crust

"Firm Nodule"

Stages ≃ 6 each one lasting ≃ 1/wk

- Stage 1: Maculopapular.
- Stage 2: Targetoid lesion.
- Stage 3: Acute weeping nodule
- Stage 4: "regenerative stage"; Nodule ē Crust ± & Black dots.
- Stage 5: Papillomatous
- Stage 6: "regressive": thick Crust covers the regressed lesion.

Spontaneous recovery ē in 3-6 wks

- Complications:
  - Scattered wide-spread Blisters.
  - Toxic Erythema after 10-14 ds.
  - EM
  - BP.

Inv:

(1.) HP:

- Epid. ⟨ pseudoepitheliomatous Hyperplasia / Central Necrosis & ulceratⁿ
- KCs: ⟨ Inclusion bodies (intracytoplasmic & Nuclear) / Vacuolizatⁿ & disaggregatⁿ of KCs
- Dense inflam. dermal Infilt.

(2) PCR: Viral Identificatⁿ in tissue Specimen

(3) DNA Hybridizatⁿ: Orf / Milker's Nodules ⟩ عشان نفرق بينهم

℞ — ??? علاجها أو ينتشر

(1.) Reassurance (Self limiting)

(2.) Sympt. ℞: Moist dressings, local Antiseptics, Finger Immobilizatⁿ, ℞ of 2ry bact. inf.

(3) Surgical: Excision, Curettage, Electro, cry for "Exophytic lesions".

(4) Recent ℞ → Cidofovir ℞. ??

Milker's Nodules

(inf. in Bovine called: Bovine papular Dermatitis)

زي الـ Orf بس خ اختلافات ← ↑ animal . Ip. . only IC, IB.

1. Virus: Milker's nodules virus (Cow Pock virus = Para Vaccinia).
2. Transmission: . From Cows (Orf = Sheeps & Goats): ⟨ Direct: Cow Teats & Calf Muzzle, / Indirect: Virally Contaminated objects
3. Ip: 4 ds – Several ws.
4. Inv. (i) Culture: on Bovine or Human Cells. (ii) PCR, DNA Hybridizatⁿ
   (iii) Elect. M: of Specimen → Viral particles.
   (IV) HP: "KCs": Ballooning, Spongiform Vacuolated Cells, W/ Pale Cytoplasm; Pyknotic Nucleus + (only) Intracytoplasmic Inclusion Bodies .... late Acanthosis. / ± Necrosis.

Molluscum Contagiosum

- Viral skin inf. Caused by poxvirus (Molluscipox) , family poxviridae.
- Etiopathogenesis:

  - Virus: Cant be cultured on artificial media but on human foreskin. There are 5 types: type 1 (95%) of infections, type 2 (3%, the most common in HIV patients), types, 3, 4, and 5. No relationship between virus type and lesional morphology or anatomical distribution is known.
  - Mode of transmission: contact (direct, indirect, autoinoculation), sexual transmission.
  - Risky patients: children, immunocompetent adults and immunocompromised (HIV, leukemia, malignancy, sarcoidosis, atopics).

C/P

- Asymptomatic, Dome-shapped, umbilicated, pearly white, small sized papules, that's if squeezed it extrude cheesy material. Both Skin and MM can be affected.
- Clinical varieties: giant MC (Lesion ⩾ 1.5 cm), disseminated (in HIV usually facial and perioral, at eczema sites of AD), eczematous MC (type of infectious eczematoid dermatitis), inflammatory MC (inflammation, suppuration, and crustation, usually not due to 2ry infection rather than traumatic).

DD

- Viral warts, KA, coccidioidomycosis, cryptococcosis, histoplasmosis, perforating dermatoses

Investigations

1. Squash preparation:

microscopic examination of cellular exudate. The cellular material contained within the central umbilication may be extracted manually, flattened between 2 microscope slides, and stained. Microscopic examination of this preparation reveals the Henderson-Paterson bodies (intracytoplasmic inclusion bodies).

2. HP: cup-shapped indentation of the epidermis into the dermis forming a crater. Within the region of the indentation, the epidermis appears thickened (acanthosis), and the cornified layer typically is disintegrated. The striking feature is the presence of intracytoplasmic, eosinophilic, granular inclusions within the keratinocytes of the basal, spinous, and granular layers of the epidermis.

These inclusions, **the Henderson-Paterson bodies**, can measure 35µm in diameter. Ultrastructural studies have shown that these bodies are membrane-bound sacs that contain numerous MC virions. The viral particles increase in size as they progress up toward the granular layer, causing compression of the nucleus to the periphery of the infected keratinocytes. The surrounding dermis is relatively unremarkable. Intact lesions show little or no inflammatory change.

TTT

1. Benign – Neglect → self limiting
2. physical Methods:
   - Curettage
   - Manual extract
   - Cryo
   - Electro.
3. Topical:
   - KOH (lo.)
   - TCA
   - Tretinoin
   - Aldara
   - Podophyllotoxin
   - Cantharidin.

Hand-foot & mouth dis (2014) (HFMD)

up.ry

Oral vesicular disorders caused by picornavirus (Echo, Entero V.) (RNA):
(i). HFMD
(ii). Herpangina
(iii). FMD

· Causative virus (Enterovirus)
(i). Coxsackievirus A16 → most common (Entero)
(ii). Cox. A6 → severe affect extend (face, perioral, limbs, eczema coxsackium) (vesiculobullous)
(iii). Enterovirus (EV-71) → sepsis (neuro-complicat.)

· Mode of Transmission (
(i) Fecal-oral route (رئيسي)
(ii) Contact c̄ infected skin lesions or oral secretions.
(3) droplet.

· C/P: . Age < 10 y. (95% < 5 y.)
. prodroma: FAHM, sore throat ± diarrhea.
. Rash: Tender/painful macules & vesicles at buccal mucosa, palate, pharynx → Hands & Feet (palms & dorsal aspects) → Erosion & ulceration. 1w → resolution
- on - Erythematous Base.
- Other area (leg, buttock, genitalia)

· Other features:
[1] onychomadesis
[2] Neurological complication (c̄ EV-71)

. Inv. (∅ is mainly clinical):
(i) leukocytosis, lymphocytosis, ↑CRP & ESR
(ii) Viral isolation: Culture, Immunoassay & PCR (detect EV-71)

. TTT → supportive measures
. Antipyretic
. Analgesic
. IV-fluid
. Amantadine & Ribavirin ??

NB ① one Hand & 2 Feet Synd → Fungal inf.
② Hand-foot Synd: pp. Erythema induced by chemoth (DNNZ)
3. Foot & Mouth dis (غير HFMD): serious, Epidemic, rare in human, Contact c̄ infected "stock". 1w → cs

Gianotti-Crosti syndrome

(PAC: Papular Acrodermatitis of childhood)

· Causative virus (1) (HBV) (ayw strain), EBV, Entero (Coxsackie A16) (أشهر), Echovirus, RSV
(HBV, EBV & vaccine — أشهر ٣)
(2) Bact. - Bartonella & Mycoplasma, strept.
(3) Vaccinat.

Age: 2 – 6 years. (6m – 12 y)

Clinically

1. Non-pruritic erythematous (dull-red, flat topped) papules (or pap. vesic) on face, buttocks and limbs lasting about 3 – 8 weeks. Fading with desquamation.
2. Enlargement of inguinal or axillary lymph nodes. (L.N), HSM, fever, ±ache
3. Acute hepatitis lasting for 2 months.

أشهر أماكن: . Extensor . Buttocks . Face
· Spare: . Trunk . Elbow . Knee . PP
→ Severe affect. is against ∅.

(أطول viral exanth. لحد دلوقتي)

. Diagnosis · clinical (اكلينيكي)
. HBS Ag.
. TTT → Conservative.

Cutaneous manifestations of hepatitis B &/or C infection (see also p. 19 in "Dermatology & Internal Medicine")
• Mixed essential cryoglobulinemia.
• Cutaneous small vessel vasculitis.
• Urticarial vasculitis.
• Porphyria cutanea tarda.
• Polyarteritis nodsa.
• Lichen planus.
• Serum sickness-like syndrome.
• Gianotti-Crosti syndrome
• Pruritus.
• Erythema nodosum.
• Erythema multiforme.

HL

Exanthema : Rash that occurs as a sign of systemic dis.

Viral exanthems

Definition

Any skin rash associated with a viral infection is called an *exanthema*. If the rash occurs on mucosal surfaces, it is termed an *enanthem*.

Causative viruses

The most frequently seen viral exanthems are those caused by: enteroviruses, measles, varicella, herpes simplex and parvovirus B19.

The virus disseminates to the skin through the blood during a viremic phase of the viral illness. The exanthema observed is the result of the local cutaneous host response to the virus. . Most viruses produce similar rashes → So / Term → Non specific Viral Rash.

Clinical types of viral exanthems and their causative viruses

1. *Widespread macular and papular eruptions (morbilliform eruptions):* Measles, rubella, HHV-6 (roseola), infectious mononucleosis (Epstein-Barr virus & cytomegalovirus) and enteroviruses.
2. *Acral-located papules (popular acrodermatitis):* affecting the fingers, toes, hands, feet, ears, nose and buttocks. Some viral infections preferentially locate to acral areas, including those that produce *the Gianotti-Crosti syndrome or popular acrodermatitis.* These viruses include hepatitis B, cytomegalovirus, Epstein-Barr virus and coxsackievirus A16. (. HBV . EBV . CMV . Cox.)
3. *Blistering eruptions on a red base* (dew drops on a rose petal): Varicella, herpes simplex, herpes zoster and coxsackieviruses (hand, foot & mouth syndrome).
4. *A widespread lacy ~~ed~~ eruption* is characteristic of erythema infectiosum: Parvovirus B19. (Lacy → Reticulated)
5. *Diffuse redness that mimics scarlet fever:* enteroviruses, adenoviruses and hepatitis B and C. (Diffuse)

Differential diagnosis of morbilliform eruptions

Viral "" → Exanthema
Drug "" → Exanthematous DE.

1 Common viruses	less common viruses	Drug eruptions 4
Measles	. Enteroviruses	Ampicillin
Rubella	. Enterovirus	Penicillin
Roseola	. Coxsackie-virus	Nonseroidal anti-inflammatory drugs
Erythema infectiosum	. Echovirus	Salicylic acid
Pityriasis rosea	Respiratory V.	Barbiturates
2 Common Bacteria	. Rhino v.	Phenytoins
Scarlet fever , SSSS, TSS	. Adeno V.	Phenothiazines
Meningococcal dis.	. RSV	Thiazide diuretics
3 Reactive erythemas	. influenza & para.	Isoniazid
Urticaria	. Parvovirus 19	Papulosquamous disorders 5
Papular urticaria	. HHV: 4, 6, 7.	Guttate psoriasis
Erythema multiforme		Graft-versus-host disease (GVHD)

Itchy → Drug
X Fever → Viral
X MM

Traditional Numbering of original 6 Exanthematous illness

- 1st dis → Measles
- 2nd → Scarlet fever
- 3rd → German Measles
- 4th → Duke's dis. (Scarlatinella)
- 5th → Erythema Infectiosum
- 6th → Exanthema subitum

STAR Complex = Sore throat Arthr. Rash.

Guidelines for Diagnosis of Exanthemas (Morbilliform)

- Trying to detect the causative virus:
  - Summer Exanthema → usually Enteroviruses.
  - Winter Exanthema → usually Respiratory viruses.

- Exanthema Acc. to the age: (حرفيا كلينكان)
  - Children
    - usually Viral
    - " Non itchy
  - Adults
    - usually Drug
    - " Itchy

- The Three main group of Viruses are
  - Enteroviruses
  - Respiratory viruses
  - Human Herpes virus gp. : HHV 4, 6, 7
    - HHV 4 → (EBV)
    - 6, 7 → (Roseola)
  - Parvovirus 19

- Discussion of some diseases caused by viruses:
  - Parvo Virus 19 Can Cause:
    - (1) Erythema infectiosum (5th dis.)
    - (2) Papular purpuric gloves & socks synd.
      - Teenagers – Young adult
      - Erythema, oedema & pruritus of hands & feet ē sharp cut off at wrist & ankles → become purpuric
      - ± ass. ē Erythema elsewhere & oral ulcers.
    - (3) Pregnancy
      - miscarriage
      - still birth
      - self limited anemia & Hydrops Fetalis.

Characteristics of

Exanth فجأة
1. Fever
1. Exanth.

"Exanthema Subitum"

Erythema Infectiosum (slapped cheek dis).
(5th dis)

- Parvovirus 19, droplet & Vertical Transmission.
- 3 Stages:

شبه الشبكة

- * (1st) → slapped cheeks: asympt Erythema affect cheeks & spare → Eyelid → Chin
- * 2nd → after (1–4 ds), Reticulated, Lacy erythema of Trunk & ext.
- * 3rd (1–3 ws) → no eruption, (but) only recur on Hot bathing, Sunlight & Exercise.

* (No MM)

Comment: Exanthema in Age < 2 ys

Roseola Infantum
(6th dis).

- IP: 1–2 ws
- HHV 6 & 7
- Age: < 3 ys (peak at 6 ms) & if affect adult it will be IM like or Hepatitis like.

*. Rash begins with drop of fever (3–5 d.)
MM

Exanthema < 2 ys → ?? تشخيص مطلوب

- Complications: Seizures & Consciousness
- Enanthema: eryth. macules at (soft) Palate; 2 ds before Exanth.

Characteristics of

Measles
(Rubeola)

- Paramyxo Virus.
- Age: < 15 ms
- IP: 9–12 ds
- prodromal (with prominent URT manif.) → Exanth. (macular or Morbilliform) at ant scalp & post auricular.
  2 ds → Spread.
- Kopliks spots: Rash بدري

LN: Post — cervical, occipital, auricular

Cluster Ø
- High fever
- Kopliks spot
- chic conjunctivitis

URT.

↑ Manifest
↓ C/o

Milder dis < Rubeola. ← German Measles

نمر ورق بالعامية

German Measles
(Rubella).

- Toga virus
- IP: 1–3 ws.
- Prodroma: FAHM & (CHIC) pain on Lat & upward Eye movem.
- (Rash): smaller < Rubeola
- Forchheimer's sign: Pinhead sized macules & Petichae on soft palate & uvula

↓ Manifest
↑ C/o

	Measles (Rubeola)	German Measles (Rubella)
. Virus	. Paramyxovirus (RNA)	Toga virus . (RNA)
. IP	. 2-3 ws .	1-2 ws
. Infectivity period .	. 5 ds before to 5 ds after rash	. 2 ds before & 4 ds after
. Prodroma	. Fever, Cough, Coryza, (Conjunctivitis)	. Children: mild - Absent . Adult: FAHM, Nusea, Pain at lat. motion [illegible] [illegible] [Painful. occipital L.N]
. Enanthema	. Koplik's Spots: grayish-white papules at eryth. background at buccal mucosa "2 ds" before & 2 ds after rash.	. Forsheimer's Spots: petichae on Hard Palate or Soft palate (Petichae → palate)
. Exanthema	. Maculopapular rash, starts postauricular & at Ant. Hair lines 3ds → spread to all over the body 5ds → [illegible]	. Maculopapular rash starts & spread caudally from face to all over the body 2-3d → [illegible] . Rash is absent in 40%.
. Complications	. OM, pneumonia . Encephalitis . . Panencephalitis ([illegible])	. Arthritis, Encephalitis, Thrombocytopenia & Cong. Rubell Inf. (if 1st Trimester) [Cataract & deafness, CHD, Anemia, Thrombocytopenia & Muffin. baby synd) "blue Berry"
ttt	(i). vaccinate (MMR; 12-15 ms) (ii). Supportive & Vit A	(i). Vaccine (ii) Supportive

(NB1) Unilat Laterothoracic Exanth. (Asymm. periflexural Exanth. of Childhood)

- Etiology ??
- prodroma (URT & GIT) → unilat. morbilliform or Eczematous rash that starts unilat (Axillae > Trunk > thigh) → spread to / Contralat. sites 3-8 w. → spont. Resolut.

(NB2) . Enteroviruses (RNA, Coxsackievirus, Echo, Feco-oral & droplet):

- HFMD & FMD
- Herpangina
- Eczema Coxsackium
- Int. organs: RT, CNS, GIT .

Pityriasis rosea

(PR)

An acute, self-limiting, papulosquamous eruption with a duration of 6-8 weeks.

Pathophysiology...??

- Viral: PR has often been considered to be a viral exanthem, a view supported by the condition's seasonal occurrence, its clinical course, the possibility of epidemic occurrence, the presence of occasional prodromal symptoms, and the low rate of recurrence upper tract respiratory infections (old speaking was regarding HHV6,7, and Picronavirus...but no evidence auggested).
- Drugs : drug induced PR.

Clinical presentation: A single scaling patch (the herald patch) appears 1-60 days before the general rash. It is an oval pink or red plaque 2-5 cm in diameter, with a scale trailing just inside the edge of the lesion. The herald patch is often mistaken as ringworm. It can also be confused with psoriasis.

A few days later, more scaly patches (flat lesions) or plaques (thickened lesions) appear on the chest and back. A few may also appear on the thighs, upper arms and neck but they are uncommon on the face or scalp. These secondary lesions tend to be smaller than the herald patch. They are oval in shape with a dry surface. Like the herald patch, they may have an inner circlet of scaling. These lesions follow the relaxed skin tension lines (Langers lines) on both sides of the upper trunk so that the rash has been described as looking like a fir tree or "Christmas tree".

PR is usually asymptomatic but may be itchy . In white skin the patches are pink or red, but in darker skin they may be pigmented or they may appear white due to the scale. Postinflammatory hypo/hyperpigm. May occur.

- Recurrence : 2% but : Relapse of fading Eupt± occur.

Clinical varieties:

- Abortive PR: herald patch only, no 2ry eruptions.
- Inverted PR: affect acral areas (face, palmoplantar...DD; $).
- Localised: cervicofacial or girdle (axillae and groin).
- Generalized .
- Segmental, unilateral and Blaschkoid
- Short course (1-2ds) & persistent PR (ms-ys, often drug induced).

- Multiple Herald Patches or No Herald Patch (2ary)

- Giant PR of vidal (pit.Circinata et marginata of vidal, limb-girdle PR): A morphologic variant characterized by atypical large patches that tend to be fewer in number and coalescent has been described. In this variant, commonly referred to as pityriasis circinata et marginata of Vidal or, the eruption generally appears in the axillae, the groin, or both, with the trunk and extremities usually spared.[32] Individual patches are 3-6 cm in diameter, exhibiting the characteristic central clearing and collarette of scale with surrounding erythema.

. Few
. large
. persistent
. Localized b... but ± generaliz...
. DD. T.Circinata

- Variations in the lesions: papular, vesicular, pustular, bullous, purpuric, urticarial, EM like, lichenoid, photoexacerbated, oral, vulval and penile.

DD:

- *2ry syphilis:* no herald patch, palmoplantar predilection, generalized LN, other manifestations, serology.
- *Pityriasiform drug eruption* (ACEI, ketotifen, bisthmus, gold, barbiturates): no herald patch, marked itching, lichenoid rash, prolonged course, postinflamm. Pigm.
- *Pityriasiform SD:* no herald patch, at midline trunk, other seborrheic areas.
- *Others:* guttate Ps.& T. corporis.

· NB: PR in 1st Trimester ± → Abort. or premature

Treatment

1. Reassurance (PPR): → self limiting.
2. Symptomatic H: Antihistamines & Topical Cs
3. Erythromycin: 250 mg X 4 /d X 2 wks (Earlier initiate → ± complete clearance)
4. NB-UVB: ↓ severity but ± → Hyperpigm.
5. Systemic Cs & Dapsone: For wide spread & Eczematous PR
6. "Acv":

EBV

1ry Inf. (IM) = "glandular Fever" → Latency → Reactivation

1ry Inf. (IM) = "glandular Fever"

- IP: 1 – 2 m.
- prodroma
  - 0 Sympt. in Children
  - Sympt. Adolescent & Young Adults. (FAHM)
- C/P (80%): Fever, L.N, Pharyngitis
- Others
  - Rash: morbilliform or Non specific ± Vesic / purpura
  - Splenomegaly
  - Tonsillitis & Hepatitis
  - Lymphocytosis c̄ Atypical lymphocytes. ← Monospot Test (نتيجة)
  - ± Petichae — eyelid / palate / cut.

Serology: Heterophil anti EBV Abs that react c̄:
1. Sheep RBCs paul Bunnel test
2. Horse " : Monospot test

Latency

- in B-lymphocytes

Reactivation

- Tm,
  - BCL
  - Burkitt lymphoma
  - Naso pharyngeal Carcinoma
- ?
  - * oral Hairy leukoplakia
  - * Hydroa Vacciniforme
  - * Necrotic Hypersensitivity to Mosquitoes Bites.
  - * Gianotti Crosti

Cut manif. of EBV

- Morbilliform
- Urticaria
- UV
- EM & EN
- PAC
- CBDC
- PLC
- Hairly leukop.
- Hydroa V.
- Annular Eyth.
- Reactive genital ulcer.

Complications

1. Common: Morbilliform rash — Ampicillin Induced Erupt. if take penicillin or Cephalosporin (Not true reaction → Safe drugs)
2. Rare: purpura, pancytopenia, encephalitis . . .

CMV

1ry Inf. → Latency → Reactivation

1ry Inf.

(1) Immunocompetent (IM like)
- IP: 1-2 m.
- C/P: IM like but
  - less Severe
  - No Tonsillitis.
  - No Heterophile Ab.
  - 33% morbilliform or petichiae.

(2) Cong & Neonatal (5–10%)
- IUGR
- Jaundice
- Thrombocytopenia
- Chorioretinitis.
- Blue-berry muffin-baby

(3) AIDs: Esophagitis, Colitis, ~~Pneumonitis~~, Chorioretinitis.

Latency

- Monocytes.
- Macrophages.

Reactivation

- Usually in Immunocompromised
- See 1ry inf.
- In AIDs & Immuno Comp.

Antiviral

- Ganciclovir
- Val "
- Cidofovir
- Foscarnet

HHV6

1ry Inf.

(6th dis) (1) Roseola Infantum (Exanthema subitum)
wic: 6ms - 2ys

- 3-5 ds fever → drop → rash
  - (Cut): Rose-red macules or papules ± surr by white Halo
  - (MM) Nagayama's Spots: red papules on soft palate

- ±
  - Palpebral Edema
  - Febrile Seizures

(2) IMN Like in Adults.

(3) Febrile Synd. without Cut. Eruption

Reactivation

↓

- DRESS
- PR

Periorbital Edema

(1) Bilat.
- ACD
- Cellulitis
- Kawasaki
- Trichinosis

(2) unilat.
- Insect bite
- Chagas dis
- Thyrotoxicosis
- unilat Conjunct.
- Retroorbital TM.

(3) in EBV: Hoagland Sign (Bilat. Eyelid Edema).

HHV7

1ry Inf.

(1). Usually Asympt., 1st 5ys of life.

(2). (±) Roseola Infantum. (less common than HHV6)

(3). ±
- Febrile Seizures
- Acute Hemiplegia

Reactivation

ع ص

- DRESS
- PR

Fever + Skin Rash.

Infect°

A. Bact:
- TSS
- SSSS
- Scarlet fever
- Septic emboli → Rickettsia, Meningococcemia
- & & ECM

B. Viral
- Enteroviruses
- Adenoviruses
- HHV6
- VZV
- HIV

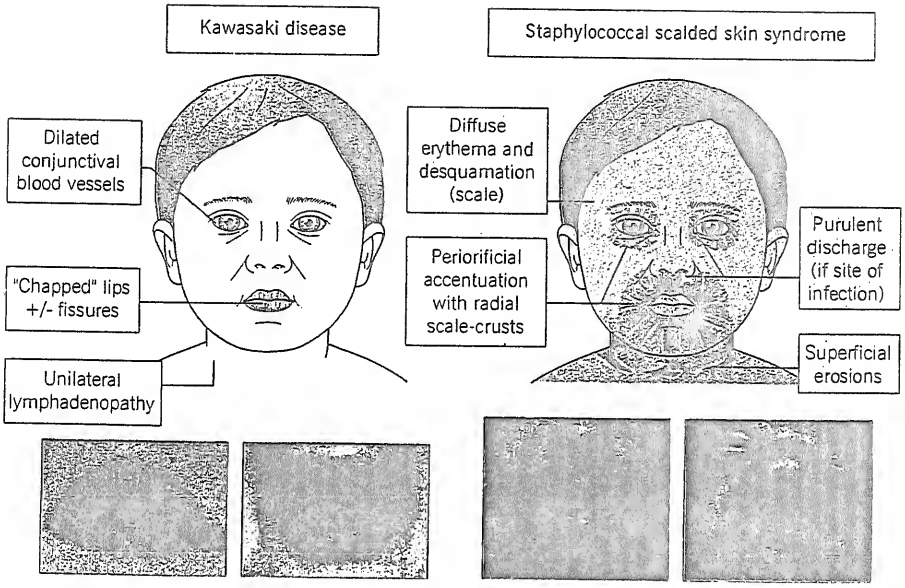
C. Fungal: Systemic Mycos

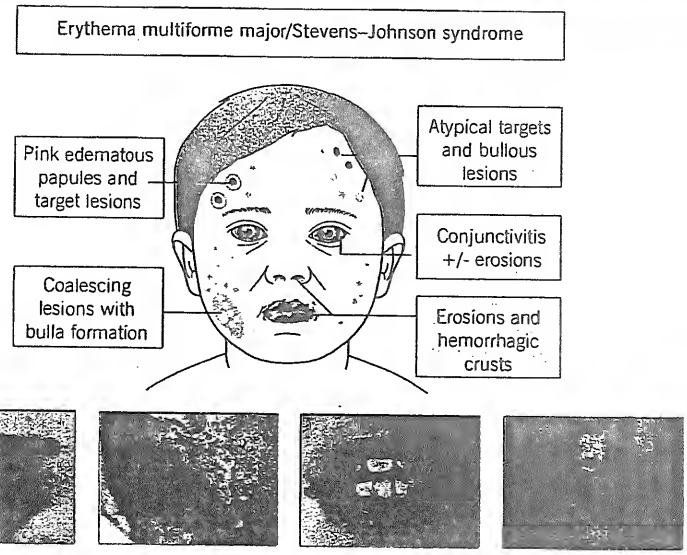
D. Protozoa: Strongyloidiasis.

Inflamm.
- GVHD
- DRESS
- AGEP
- SJS/TEN
- EM
- Serum sickness like Reac°
- AICTDs

Others
- Kawasaki
- Periodic fever Synd.
- Lymphoma..

FACIAL FINDINGS IN KAWASAKI DISEASE, STAPHYLOCOCCAL SCALDED SKIN SYNDROME AND ERYTHEMA MULTIFORME MAJOR/STEVENS-JOHNSON SYNDROME





Severe Cut. Adverse React= (SCAR)

- DRESS
- SJS/TEN
- AGEP
- Drug induced Erythroderma

DRESS = DHS (drug Hypersensitivity Synd) → (or Anticonvulsant HS)

Drug intake "Anticonvulsant"

- Most Common: Aromatic Anticonvulsants:
  - Carbamazepine
  - phenytoin
  - phenobarbital
- Antiepileptics, Allopurinol, Sulfonamides → (أشهر)
- Others: Sulfa, Allopurinol, Azath., Dapsone, Terbinafine.

onset:
- أول مرة بأخذ الدوا (2 - 8 Ws) — فترة طويلة مقارنة بالأنواع الأخرى من DE.
- ثاني مرة كمان → 1 day.

↓

• Fever • Rash • L.N • Pharyngitis • Facial oedema

- Rash (90%): Most Common: Morbilliform (90%)
  - Others: Erythrodermic, Urticarial, Bullous (SJS/TEN like; but Not d.t. KCs Necrosis but d.t. Cut. Edema); Pustular; Targetoid.
- L.N (75%): Painful either < local Cervical or Generalized.
- Pharyngitis (25%): pharyngeal, oral, labial ulcerat= or Strawberry Tongue (± genital).
- Facial oedema (30%) (or Angioedema) → DE مساعدة هامة للتشخيص لأن أغلب الأمراض لا تؤثر على الوجه
  - Sign of Severe systemic affect=.

↓

Int. organ affect= sp. . Liver . Blood . Kidney . others (MR 20-40%)

- Hepatitis (70-90%): ↑enzs, ± fulminant.
- Blood (50%): Leucocytosis ē < Eosinophilia (80%), Neutrophilia, Atypical lymphocytes.
  - Anemia & thrombocytop.
- Others: Nephritis, Carditis, Pneumonitis, Myositis, GIT, Encephalitis, Thyroiditis.

Criteria of diagnosis of DRESS

1- The European Registry of Severe Cutaneous Adverse Reactions to Drugs and Collection of Biological Samples (RegiSCAR) :require at least 3 of the following:

- Hospitalisation
- Reaction suspected to be drug related
- Acute skin rash
- Fever about 38 Celsius
- Enlarged lymph nodes at two sites (≥2)
- Involvement of at least one internal organ (≥2)
- Blood count abnormalities such as low platelets raised eosinophils or abnormal lymphocyte count.

↑ WBCs
↑ PLTs.

2. Japanes Criteria: (7 = Typical DRESS; 5 = Atypical DRESS.)

- Maculopapular Rash develops ≥ 3 ws after drug.
- Prolonged clinical symptoms ≥ 2 after stop ″.

other
- Facial Edema
- pharyngitis

- Fever > 38 °C
- L.N
- Leukocytic Abnormalities → leukocytosis (>11000); Eosinophilia (>1500); Atypical lymphocytosis (>5%)
- SGPT > 100 U/L.
- HHV6

Diagnosis

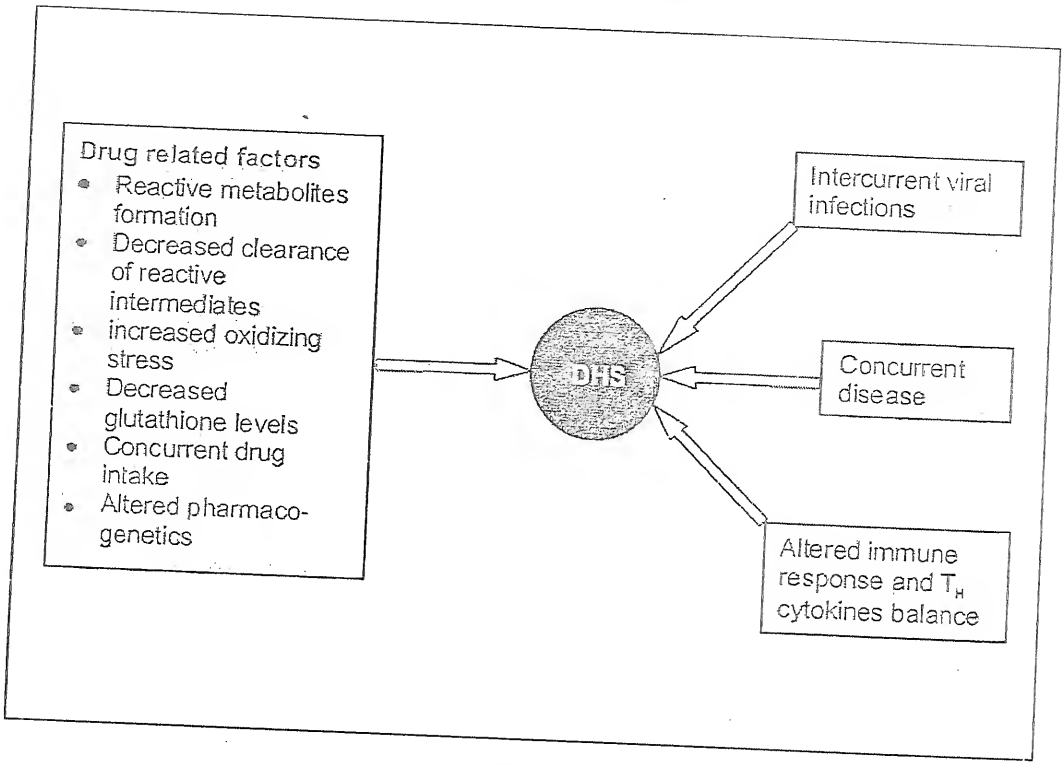
(i) HP
- Perivascular infil. < dense; superficial
- Spongiotic or lichenoid dermatitis.
- Dermal Edema
- LN: Pseudolymphoma like ē Atypical cells.

(ii) Lymphocytes Toxicity Assay
نقيس تأثير الدواء
على WBCs مرضى

Patch testing
مفيد في حالات
. 50% +ve ē Anticonvuls.
But -ve ē Allopurinol.

Diagnosis	Rash	Onset	Fever	Internal organs	Arthralgia	Lymphadenopathy
DHS/DRESS	Exanthematous. Exfoliative dermatitis. Urticarial plaques. Pustular eruption. SJS-TEN	1-8 weeks	Present	Present	Absent	Present
Pseudolymphoma	Single or multiple nodules	6 months	Absent	Absent	Absent	Present (biopsy shows atypical hyperplasia simulating malignancy)
Serum sickness-like reaction	Urticarial. Exanthematous	7-14 days	Present	Absent	Present	Present

ETIOPATHOGENESIS



TTT

A. **Patients with non–life-threatening or non–organ-threatening disease**

Discontinue anticonvulsant

Supportive therapy (e.g., antihistamines, topical corticosteroids)

Obtain complete blood count, carry out liver function tests, urinalysis, serum creatinine, baseline thyroid function tests, other tests based on symptom presentation

Skin biopsy, if blistering or pustular eruption

Advise patient regarding potential for cross-reactivity

Counsel family members and first-degree relatives regarding increased risk

Advise patient to obtain a MedicAlert

B. **Patients with life-threatening or organ-threatening disease**

All the above measures *plus*

Use of oral prednisone or pulse methylprednisolone

Intravenous immunoglobulin and cyclosporine can be used as alternatives or adjuvants

Vaccines in Dermatology

• HPV → جدول أول عام

TB

(1). BCG (Bacillus Calmette G.)
(2). live attenuated (LAV)

. الجرعة: أول يحقن بالجلد بعد الولادة أو بعد ذلك لو عنده خطر العدوى

. استعمالات أخرى: تحسين المناعة في حالات السنط وسرطان البروستاتا

Leprosy

(1). BCG
(2). BCG + Killed M. leprae (ConVit)
(3). Tawalars (M. welchii strain)
(4). Subunit Vaccine.

. يعطى لأي حد معرض للعدوى
. أو عايش في منطقة Endemic

HSV (under trial)

. Killed whole vaccine
. LAV
. Recombinant Glycosylated subunit.

أي حد معرض للعدوى .. للذي واخد اللي هي Sero -ve وجوزها +ve

Varicella ← طبعا معروف ..

(1). VariVax] LAV
(2). MMR-V

. يعطى في سن ١٢-١٥ شهر
. ويكرر عند ٤-٦ سنوات

→ prevent infection or severe attacks
→ ↓ incid. of PHN

HBV

○ Subunit.
○ Recombinant.

* 3 IM doses at: 0, 1, 6 m.

أي حد يتعامل مع دم أو معرض للعدوى زي الغسيل الكلوي

HIV (under trial)

. AIDSVAX : gp120 subunit.
. Subunit
. Recombinant

. أي حد معرض للعدوى (طبعاً معروفين)
. ليه صعب تصنيعه بقى كليتشي نظري في كتاب STDs

MMR

. LAV
. Dose: as Varicella

Acne

- "Component" Vaccine..
- "Inactivated" Whole Bact.

ss (بيشتغل ازاى)

↓ IL8 & MIP2 (macrophage Inflammatory protein) Released By P. Acnes.

Melanoma

- Whole Cell Tm Vaccines
  - Autologous Tm Vaccine
  - Allogenic " "
  - peptide Vaccines
  - Ganglioside "
- Idicats: Metastatic Melanoma.

يحقن عضل او تحت الجلد او بالحبل
فى اى Limb بيعمل الا فير MM

- "HPV"
- "Leishmania"

HPV Vaccines

Why HPV is dangerous?	-HPV is Highly oncogenic.. Virtually all cases of cervical cancer, 95%cases of anal cancer &70 % of oropharyngeal cancers are due to HPV. - Dozen high-risk HPV types have been identified. Two of these, HPV types 16 and 18 (16>>18). -HPV 6&11 are responsible for 90%of genital warts. - CDC :estimates that more than 90 % and 80 %, respectively, of sexually active men and women will be infected with at least one type of HPV at some point in their lives . Around 50% are with a high-risk HPV type. - Most high-risk HPV infections occur without any symptoms, go away within 1 to 2 years, and do not cause cancer. Some HPV infections, however, can persist for many years. Persistent infections with high-risk HPV types can lead to cell changes that, if untreated, may progress to cancer.
Mechanism	- HPV vaccines are based on virus-like particles (VLPs) that are formed by HPV surface components (Major capsid protein L1). (Purified protein prod.) ✓ - VLPs are not infectious, because they lack the virus's DNA. However, they closely resemble the natural virus, and antibodies against the VLPs also have activity against the natural virus
Types	- Cervarix or bivalent vaccine: (HPV:16,18): FDA (2009) - Gardasil 4 or quadrivalent vaccine: (HPV:6,11,16,18): FDA (2006 In females&2009 in males) - Gardasil 9 or nonavalent vaccine : (as G4+HPV 31, 33, 45, 52, and 58): FDA (2014).

(Attenuated)	Killed	Purified
. Measles . Mumps . Rubella . BCG . VZV	. Typhoid . Rabies . Cholera . HAV	. HPV . HBV . Diphtheria . Tetanus .

Indications	The Advisory Committee on Immunization Practices (ACIP), recommendations: - Initiation at age 11-12 years (but can be at 9 years) - Females aged 13 -26 years and males aged 13-21 years who have not been vaccinated previously or who have not completed the three-dose vaccination series. - Males aged 22 through 26 years may be vaccinated. - Vaccination through age 26 years of men who have sex with men and for immunocompromised persons if not vaccinated previously
Dose (IM)	- WHO: two doses, 6 months apart - US: 3 doses at 0, 2, and 6 months
Efficacy	- Gardasil and Cervarix: provide nearly 100 % protection against persistent cervical infections with HPV types 16 and 18 and the precancerous cervical cell changes - Gardasil 9: is effective as Gardasil as regard HPV4 Types, and 97 % effective in preventing cervical, vulvar, and vaginal disease caused by the five additional HPV types (31, 33, 45, 52, and 58).
Duration of protection	Gardasil for 8ys, Cervarix for 9ys
Efficacy	- Gardasil and Cervarix: provide nearly 100 % protection against persistent cervical infections with HPV types 16 and 18 and the precancerous cervical cell changes - Gardasil 9: is effective as Gardasil as regard HPV4 Types, and 97 % effective in preventing cervical, vulvar, and vaginal disease caused by the five additional HPV types (31, 33, 45, 52, and 58) that it targets
When to start sex after vaccination?	Sex should be avoided till completion of the 2 or 3doses (after 6ms)
Can we give them in already infected persons?	- HPV vaccines are safe when given to people who are already infected with HPV, the vaccines do not treat infection. They provide maximum benefit if a person receives them before he or she is sexually active. - It is likely that someone exposed to HPV will still get some residual benefit from vaccination, even if he or she has already been infected with one or more of the HPV types included in the vaccines.

	- At present, there is no generally available test to show whether an individual has been exposed to HPV. The currently approved HPV tests show only whether a person has a current infection with a high-risk HPV type at the cervix and do not provide information on past infections.
Can we give them in those having cervical cell changes?	- Yes , should still receive HPV vaccination if they are in the appropriate age group because the vaccine may protect them against high-risk HPV types that they have not yet acquired. – Neither treat the already HPV inf. Nor the abnormal Pap test
After vaccination, is Pap smear still important?	Yes. Because these vaccines do not protect against all HPV types that can cause cancer, screening continues to be essential to detect precancerous changes in cervical cells before they develop into cancer. In addition, cervical screening tests—HPV DNA test alone, or HPV and Pap test together, also known as co-testing—are critically important for women who have not been vaccinated or who are already infected with HPV.
Adverse effects	- Most were minor and not greater than background rates compared with other vaccines, the exception being higher rates for syncope (is it from injection or vaccine..???any way; Patients should remain seated for 15 minutes after injection) and **thromboembolism** (0.2cases/100.000). - Other adverse events include local site reactions, headaches, hypersensitivity reactions, and urticaria.
Does Gardasil Increase Risk of Precancerous Lesions, or Worse?	- According to Information the manufacturer of this vaccine presented to the FDA prior to approval, if a person has already been exposed to HPV 16 or 18 prior to injection Gardasil increases the risk of precancerous lesions, or worse by 44.6%. - Is this information advertised? No! This information was actually presented to the FDA by Merck. It came from their own safety trials. The FDA did not respond by recommending screening for HPV prior to vaccination. The FDA did not even demand a warning be included in the package insert. - Now, Merck's research is indicating that Gardasil may also "provide cross-protection" against other strains of HPV that are closely related to HPV 16 and 18. (see this article on Medpage Today) This means prior exposure to these additional strains may pose an increased risk for cervical cancer also, if combined with vaccination - No one appears to be concerned with the increased risk of vaccination combined with prior exposure, as long as you take the vaccine. You will see no advertisements indicating the possibility of increased risk of the very cancer this vaccine is supposed to help you avoid.
Price	$130 to $160 per dose

(ملخص) نقاط مهمة

(1). HPV
- 100% Cancer Cx
- 95% " anus
- 70 oropharyngeal.

(2). Vaccine: purified product Major Capsid protein L_1 — تصنيع

(3). Efficacy
- persistent Inf (100%)
- precancerous & cancerous lesions of C.Cx (97-100%)
- Valvar & Vaginal Cancer (Gard p)

(4). ممنوع معاشرة الا بعد ٣ جرعات (WHO (مرحلية فقط))

(5). (Inf. تطعيم المصابة)
- لا يعالج.
- pap. لا يغير. لو اتغيرت
- تطعيم لو عندها عدوى لسببين
  1. Residual effect
  2. protect by others types who havn't catched by the pt.; also cross activity

(6). نتيجته تمتد لفترة ٨-٩ سنوات

(7). S.E:
- Rach: pain, Erythema, Swelling, pruritus, urticaria
- Syncope
- Thromboembolism.

Cervarix (2)	Gardasil (4)
No protect against 16,18 Genital warts	protect.
0.5 ml, IM: 0, 1, 6 m.	0, 2, 6 m.
Age approval: ♀ 10-25 y.	♀: 9-26; ♂: 9-15
Catch-up: 8-25 y.	8-26 y.
Elderly: ♀ 26-55	Not recommended for ♀ > 26
~~Cross protect: HPV 31 & 45~~	